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No Evidence for Altruistic Analgesia via Effort-Based Prosocial Behaviour

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No Evidence for Altruistic Analgesia via Effort-Based Prosocial Behaviour

Prosocial behaviour in the form of helping, cooperation and altruism is paramount for a functional social group. While the benefits of, for example, maternal care, donating, or volunteering for greater society are well understood, the positive effects on the prosocial actors themselves are often overlooked. Sociobiologist Edward O. Wilson (1975, p. 578), for example, defines altruism as "[…] self-destructive behaviour performed for the benefit of others.". On the contrary, a long line of research suggests that prosocial behaviour does not only benefit the receiver but also the actor in different ways beyond social reward and societal reciprocity (Andreoni, 1990; Aknin et al., 2018; Brown & Brown, 2015; Inagaki et al., 2016; Inagaki et al., 2022; Penner et al., 2005). Specifically, prosocial behaviour seems to hold intrinsic advantages for the prosocial actor, such as stress reduction (Penner et al., 2005; Lazar & Eisenberger, 2022; MacCormack & Muscatell, 2022), general positive feelings (Aknin et al., 2018), an increased perception of meaning in life (Klein, 2017) and improved mental as well as physical health (Brown & Brown, 2015; Haroz et al., 2013; Mogil, 2021; Schreier et al., 2013; Schwartz et al., 2003). Aknin et al. (2013), for example, investigated the impact of prosocial financial spending across different nations as well as cultures and found that people experienced more happiness after prosocial spending compared to self-benefiting spending. They also observed a general correlation between subjective well-being and prosocial spending across the 136 countries examined. Raposa et al. (2016) likewise found that self-reported prosocial behaviour was associated with a reduction in negative effects connected to daily stressors. Similarly, Harris et al. (2005) reported a significant reduction in mortality of volunteers compared to non-volunteers. Furthermore, there seems to be a connection between prosocial behaviour and a decrease in pain perception (Macchia, Farmer, & Kubzansky, 2023; Wang et al., 2020). In a recent longitudinal study conducted in the UK, Macchia, Farmer, and Kubzansky (2023) found that participants engaging in self-reported money donations and volunteering reported significantly less pain interference over a 10-year period compared to participants who engaged in less or no prosocial behaviour.

However, so far, most of the research concerning the positive effects of prosocial behaviour has taken a holistic approach, looking at long-term effects of general prosocial behaviour like volunteering work and financial helping (Penner et al., 2005; Haroz et al., 2013; Harris & Thoresen, 2005; Hooten, 2016; Inagaki et al., 2022; Macchia, Farmer, & Kubzansky, 2023; Macchia, Plagnol, & Powdthavee, 2023; Mogil, 2021). This approach, however, limits the ability to draw inferences about the mechanisms underlying such effects,

given that unmeasured confounding factors may account for the observed relationship. For instance, volunteers have been observed to exhibit a significantly higher amount of general physical activity compared to non-volunteers (Varma et al., 2016), which is a well-established determinant for general health (Malm et al., 2019). There are also a number of possible mediating factors, like social support, with social support reducing pain perception (Weiß et al., 2024) as well as being a driver of prosocial behaviour and general health (Kumar et al., 2012; Uchino et al., 2016), which makes conclusions of a direct causal connection difficult, since the observed positive effects could be mediated by broader factors rather than factors specific to prosocial behaviour itself. However, recent experimental evidence indicates that there might not only be a direct causal connection between prosocial behaviour and analgesia, but that this analgesia might also be linked to meaning-related processes.

The Analgesic Effects of Prosocial Behaviour

One of the most comprehensive pieces of evidence for what they termed *altruistic analgesia* comes from a recent research project conducted by Wang et al. (2020). Over the course of two pilot studies and three experiments, Wang et al. (2020) provide behavioural alongside neuronal evidence, that prosocial behaviour might have a direct effect on the prosocial actors' pain perception.

In the first pilot study, they observed that blood donors reported significantly reduced pain intensity (using a Wong–Baker Faces Pain Rating Scale (Wong & Baker, 1988)) during the blood drawing procedure compared to people providing a simple blood sample. In the second pilot study, they further found that people who voluntarily decided to revise a children's book reported less pain intensity when exposed to a cold pressure test paradigm, compared to people who decided against the prosocial act. These findings illustrate that the observations from the first pilot study could be recreated using a standardised experimental pain paradigm. Building onto these two preliminary pilot studies, they conducted additional standardised experiments.

In the first of the experiments, participants were split into two groups, both answering a survey, which either provided them with a monetary reward or donated the money to a charity. Participants in the donation group reported significantly less pain intensity during a tourniquet pain test compared to participants who received the monetary reward themselves. In the second experiment, participants either decided to donate or refuse to donate money to orphans during the experimental condition. They additionally compared the shapes of figures in the control condition. After each trial an electrical shock was applied to the participant's

hand, and pain intensity was rated on a visual analogue scale (VAS). Similar to the pilot studies and the first experiment, participants reported significantly less pain after the altruistic condition compared to the control condition. Additionally, they used functional magnetic resonance imaging (fMRI) to investigate the underlying neural substrates of this effect. They found that activation of the ventromedial prefrontal cortex (vmPFC) was negatively correlated with activation of affective as well as somatosensory brain areas connected to pain (specifically the anterior cingulate cortex (aCC), the anterior insula (AI) and the primary somatosensory cortex (S1)). Moreover, they discovered parallel functional connectivity between the vmPFC and AI during prosocial behaviour, suggesting an effect on the pain-related brain areas even without the presence of a nociceptive stimulus. After the task, participants were further asked to rate how meaningful they perceived their donation behaviour. These meaningfulness ratings predicted reduced AI activation during the pain stage, while vmPFC activation during donation predicted the subsequent meaningfulness ratings.

Another recent study by López-Solà et al. (2018) further supports the role of the experience of meaning as well as the vmPFC in prosocial behaviour-based pain modulation. They found that choosing to endure thermal pain on behalf of a loved one reduced pain unpleasantness ratings through affective meaning and increased vmPFC as well as reduced AI activation during pain reception. Likewise, they found that willingness to receive the painful stimulus mediated the extent of the unpleasantness reduction and vmPFC activation.

Similarly, Chen et al. (2024) found that costly helping to avoid the pain of others led to reduced activity of pain-related brain regions during vicarious pain experiences. Considering that the affective experience of pain and vicarious pain overlap on a neural level (Lamm et al., 2011, Rütgen & Lamm, 2022), this supports the notion that prosocial behaviour can influence the experience of pain on a neuronal level.

The abovementioned findings are consistent with a growing body of evidence establishing the ventromedial prefrontal cortex (vmPFC) as a central hub for computing subjective value and affective meaning in social contexts (Cooper et al., 2010; Koban et al., 2017; Roy et al., 2012). Through its connectivity with descending pain pathways and affective brain areas (Fauchon et al., 2019; Hashmi et al., 2014; Martucci & Mackey, 2018; Motzkin et al., 2023; Woo et al., 2015), it is also uniquely situated as a hub of top-down pain modulation. Specifically, the vmPFC seems to play a vital role in social cognition-based pain modulation (López-Solà et al., 2024; Sharvit & Schweinhardt, 2022).

Moreover, meta-analytic studies show that the vmPFC is consistently activated across prosocial decision paradigms, including altruistic giving and cooperation tasks, reflecting integrated valuation of outcomes for others beyond empathy or theory of mind alone (Bellucci et al., 2020; Cutler & Campbell-Meiklejohn, 2019; Yang & Li, 2025). A recent lesion study by Lockwood et al. (2024) showed that lesions in the vmPFC led to a reduction in prosocial decisions during an effort-based decision task, further emphasising the causal role of the vmPFC during prosocial decision-making.

Taken together with the aforementioned evidence, prosocial behaviour seems not only to reduce pain ratings and pain-related neural activity, but this analgesia also seems to be mediated by increased vmPFC activation driven by meaning-related processes. With the experience of meaning itself being indicated to reduce pain intensity (Boring et al., 2014), altruistic analgesia seems to be working through the integration of affective meaning experienced during prosocial behaviour with vmPFC activation leading to a downregulation in descending pain pathways as well as the brain areas connected to the affective experience of pain.

However, a lot of the modalities and attributes of this analgesic effect are still unknown. For example, there is, up to this point, no research investigating how different characteristics of prosocial behaviour, like effort investment, outcome and the sheer number of prosocial choices, influence this analgesic effect.

The Possible Role of Effort Investment and Outcome Magnitude in Altruistic Analgesia

Prosocial behaviour is generally connected to a resource or effort cost, be it donating to a charity, picking up trash from the sidewalk or volunteering at a soup kitchen. However, it is as yet unknown how this cost interacts with prosocial meaning and, in turn, the aforementioned analgesic effect.

When it comes to general valuation processing of choices, effort can lower the perceived value of a choice (Botvinick et al., 2009; Vinckieer et al., 2022; Zhang et al., 2015), especially for prosocial behaviour (Lockwood et al., 2017). Lockwood et al. (2017), for example, found that participants were less willing to exert effort for the monetary gain of others compared to self.

However, while effort investment might diminish the economic value of a choice, recent research indicates that investing effort can indeed increase the experienced meaningfulness/affective valuation of a task and its outcome (Inzlicht et al., 2018; Wang et al., 2025; Lallement et al., 2014). Olivola & Shafir (2013), for example, observed what they call the 'Martyrdom Effect'. This effect describes the phenomenon that people perceive

prosocial acts as more meaningful if they are connected to effort and pain. Further, Campbell et al. (2025) observed that the extent of effort invested into a task increased the perceived meaningfulness of the task and outcome beyond post-hoc effort justification. This indicates that while effort can generally decrease the attractiveness and perceived economic value of a choice, exerting effort increases the perceived meaning of the prosocial act and its outcome. In turn, investing more effort should lead to a more pronounced analgesic effect of prosocial behaviour.

When it comes to variation in outcome itself, there are no studies specifically investigating how outcome magnitude influences altruistic analgesia. However, a wide variety of research indicates that higher reward magnitude leads to an increased motivational valuation of prosocial behaviour (Engel, 2011; Lockwood et al., 2017; Lockwood et al., 2024), especially in a scenario where the pain of others can be avoided (Crockett et al., 2014). Further, primary reward-related vmPFC activation has been shown to increase with reward magnitude (see Hélie et al., 2017 for review). Importantly, prosocial reward processing engages similar neural valuation systems as primary reward, including the vmPFC, indicating similar reward processing to intrinsic reward (Kroker et al., 2024; Zaki & Mitchell, 2016). Consequently, prosocial reward magnitude should similarly influence valuation-based vmPFC activation. Combining these findings, higher prosocial reward magnitude should in turn also increase the analgesic effect of prosocial behaviour through an increase in meaning/valuation-related vmPFC activation.

Interestingly, the vmPFC seems to be more active during the feedback, meaning the experience of the outcome of rewarding behaviour, compared to decision-making (Vanessa et al., 2014). However, prior research has not investigated during which phase of prosocial behaviour meaning-related vmPFC activation arises and how it relates to the analgesic effects and the downregulation of pain-related brain areas. As aforementioned, the vmPFC is not only engaged during economic valuation at choice but also reflects meaningful integration of outcome significance and self-relevant value. In social contexts, this meaning may arise both at the moment of choice and during outcome evaluation when individuals experience the consequences of their prosocial actions (e.g., López-Solà et al., 2018; Kim & Johnson, 2015).

Aim of this Study

Taken together, the aforementioned studies point towards an analgesic effect of prosocial behaviour. This effect may arise, in part, due to meaning-based activity in the vmPFC during prosocial acts, with the vmPFC also being implicated in top-down modulation of pain. However, so far, studies have not included varying degrees of effort, quantitative

variations in outcome magnitude as well as prosocial choices during the same task. Further, to my knowledge, there is no research on how effort-based, prosocial pain avoidance behaviour influences pain perception and if the altruistic analgesic effect can be replicated using a prosocial effort task.

This thesis aims to explore how variation in effort level, prosocial reward level (outcome) and number of prosocial choices affect pain perception during a repeated-measures study design. Further, this thesis aims to investigate how vmPFC activation during a prosocial effort task influences pain perception and its neural substrates using functional imaging data.

Hypotheses

Behavioural Hypotheses

Hypothesis 1a: A higher number of prosocial choices will predict lower pain ratings.

Hypothesis 1b: A higher level of prosocial reward (higher shock reduction) will predict lower pain ratings.

Hypothesis 1c: A higher invested level of prosocial effort will predict lower pain ratings.

Neuronal Hypotheses

Hypothesis 2a: Higher vmPFC activation will predict lower pain ratings.

Hypothesis 2b: vmPFC activation during prosocial choice and outcome feedback will negatively covary with neural activity in affective pain networks (AI, ACC).

Hypothesis 2c: vmPFC activation during prosocial choice and outcome feedback will negatively covary with neural activity in the primary somatosensory cortex (S1).

Methods and Materials

Ethics

This study included deception in the form of a confederate, a supposed second participant that would conduct the experiment alongside the real particapant. In reality, the second participant (confederate) was part of the research team. After the experimental procedure, participants were debriefed on the deceit alongside the detailed aims of the experiment. The study was conducted in accordance with the Declaration of Helsinki (World Medical Association, 2024) and approved by the ethics committee of the University of Vienna. All participants signed a form agreeing to participate (see Appendix B) in the study and were screened and educated on the risks of MRI scans as well as the methods used to induce acute sustained pain.

Sample

This study includes a subsample of a larger research project, comparing empathic responses and prosocial behaviour between a group of participants undergoing acute sustained pain and a control group. Since this thesis exclusively aims to investigate the effect of prosocial behaviour on pain perception, it solely focuses on the experimental group.
The overarching larger research project aimed for a sample size of 72 participants, with 15% of oversampling accounting for post-hoc exclusions. The experimental group data included 39 participants. After quality checks and manipulation checks (see sections Quality Checks & Manipulation Checks), the final sample used in this master's thesis consisted of 30 participants (Agerange = 19-39, Agemean = 26, AgeSD = 5.48558, F = 21).
Participants were awarded 50€ for participation in the study. Recruitment was mainly achieved through online advertising, flyers and the Vienna CogSciHub: Study Participant Platform (Bock, Baetge, & Nicklisch, 2014).

Exclusion Criteria

The following table (Table 1) includes all pre-experimental exclusion criteria, which were defined beforehand.

Table 1

Exclusion Criteria

Recent Drug Use
Alcohol/Drug Dependencies/Addictions
Non-Removable Metal Piercings
Facial Tattoos
Left-Handedness
German Fluency Below A2 Level
Psychology Students
Current Pregnancy
Chronic Pain
Current Health Issues
Lasting Psychiatric/Neurological Disorders

Design and Procedure

Interested volunteers were screened for eligibility via a short online screening questionnaire. Eligible individuals were then invited to the experimental sessions at the laboratory (MR-Centre of the Faculty of Psychology at the University Clinic of Dentistry – MedUni Vienna). Upon arrival at the laboratory, participants were introduced to a confederate, posing as a second participant partaking in the experiment alongside them. To avoid interactions of study outcomes with confederate gender, all confederates were female.

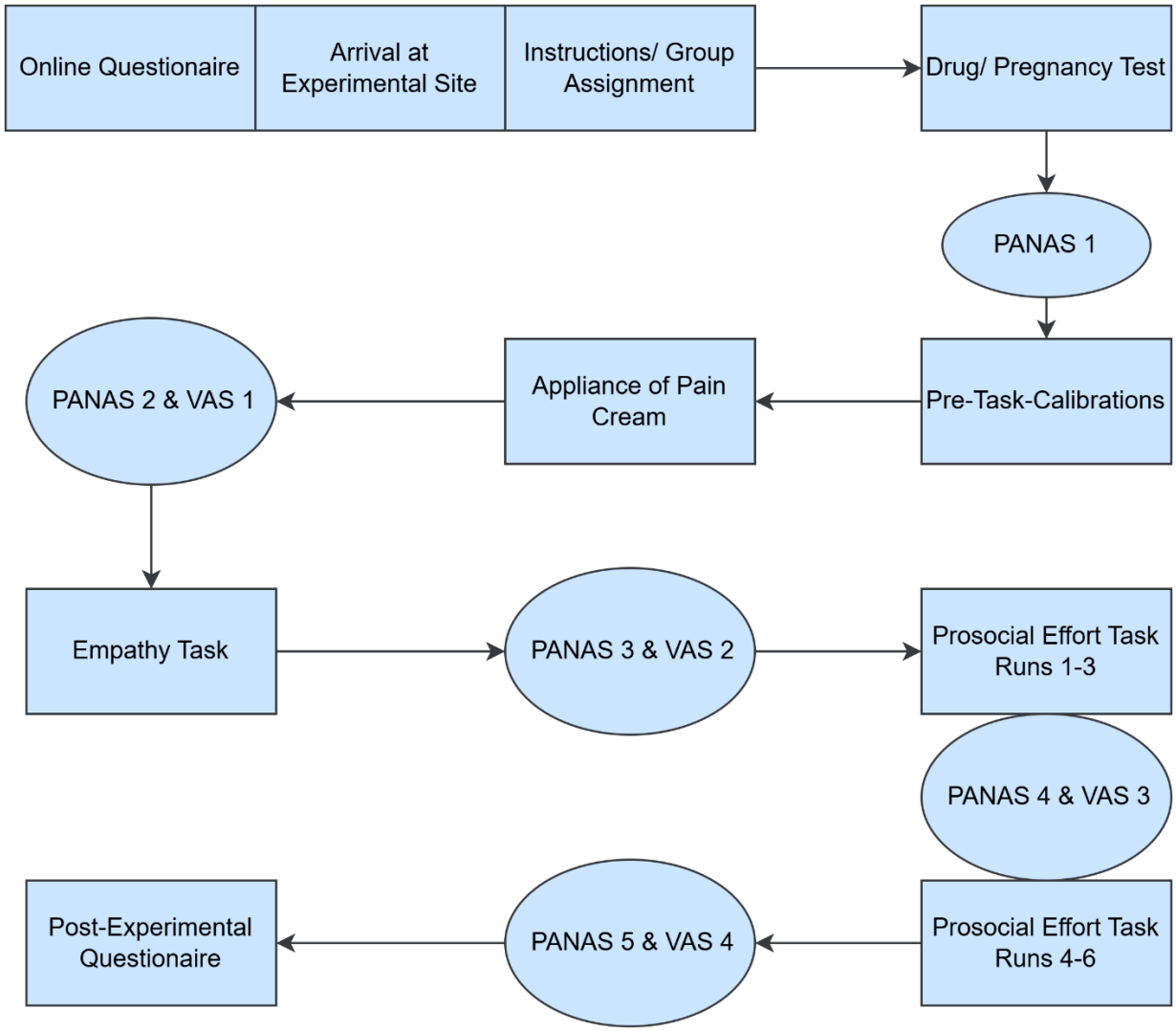
After a short introduction, participants and confederates underwent the same consent and MRI safety procedure and were pseudo-randomly assigned to groups (sustained pain group vs control group – the latter not included in this thesis), with participants being told they were assigned to the group that would perform the experiment inside the scanner, while the confederate would participate in the experiment outside of the scanner in the scanner room. In actuality, the confederate would visibly enter the scanner room and sneak out again right away, shortly before the main tasks were conducted. Following an instruction of the experimental procedure, drug and pregnancy tests were performed. In case of either a positive drug or pregnancy test, the experiment would be stopped, and the participant would be excluded. Afterwards, the participants and confederates were separated, with the participants being told that both they and the confederates would complete the same pre-measures and calibrations. Following the separation, the participants were again briefed on the MRI safety measures, and a 5x5 cm square was marked on the left forearm. Subsequently, the

participants were put into the scanner, and their maximum voluntary contraction (grip strength, MVC) and pain threshold were calibrated. To keep data consistent throughout the experiment, both grip strength and individual pain threshold calibrations were conducted with the subject inside of the scanner. Succeeding the calibrations, the pain cream was applied in the previously marked area. For the experimental group, 3 ml of a heat-inducing cream was applied to the inside of the left forearm (Rubriment®), wrapped tightly in cling wrap, creating a constant painfully hot sensation. While the pain cream took effect, scanner settings were performed. The first pain rating was taken 15 minutes after the application of the heat cream. Next, the two main tasks were performed. First, an empathy-for-pain paradigm, not related to this thesis, followed by a prosocial effort task was completed**.** Before, throughout and after the tasks, further pain ratings and affect ratings were taken (see Figure 1 and Analysis section).

Following the task, participants' grip strength was measured again, and they were asked to fill out a post-experimental questionnaire including questions on legitimacy and confederate perception (see Appendix C).

Figure 1

Experimental Procedure



Note: Full experimental procedure including pre-experimental online screening. The empathy task and the accompanied pain sensitivity calibration mentioned here were part of the overall larger research project, however, are not part of this master's thesis. Visual Analogue Scale (VAS) 1- 4 represent the timepoints of the pain measure. Since only data from the prosocial effort task is analysed, only VAS 2-4 are used as pain measure in the analysis. The Positive and Negative Affect Schedule (*PANAS*, Krone et al., 1996) was used as positive affect measure, however, is not analysed in this thesis (For detailed pre- and post-questionnaire information, see Tables D1 & D2)

Maximum Voluntary Contraction (MVC) Calibration

Maximum Voluntary Contraction (MVC) is a common approach to measuring muscle strength in research. It represents the greatest amount of force a person can voluntarily produce with a certain muscle or muscle group. To calibrate effort requirements for our tasks, the maximum grip strength of each participant was collected. Participants were asked to grip the hand-dynamometer with their right hand as hard as they could, filling up a virtual bar based on contraction intensity (see Figure 3).

Figure 2

MVC Calibration Setup

Note: Schematic Set up of the MVC calibration used in this study

Prosocial Effort Task

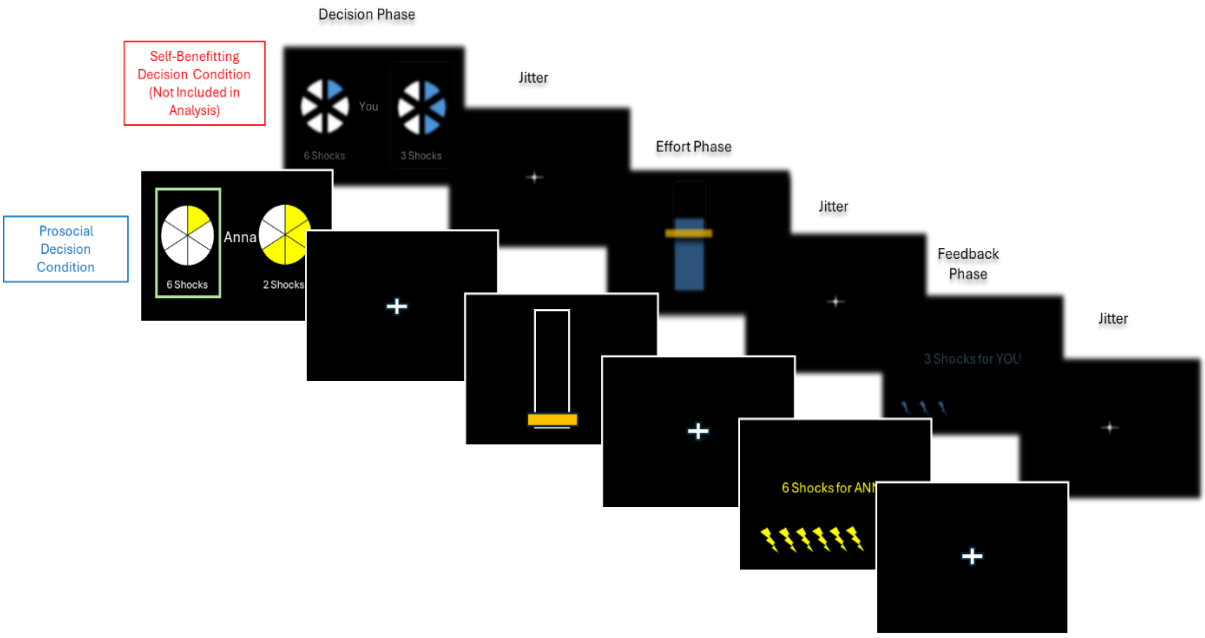
To assess prosocial effort, an adapted version of the prosocial effort task by Lockwood et al. (2017) was used. In this version participants were told that both they themselves and the confederate would be carrying out a task in which their decisions on whether to exert effort or not (effort or no effort choice) would influence the number of painful electrical stimuli applied to themselves and the other person post-task. In each trial, participants were presented with an effort or a rest option. Choosing the rest option would always save 6 shocks, and no effort exertion was required. The effort option always had a reward level (reduction of shocks saved, 1-5) and an effort level (40%-80% of MVC) allocated to it. Both effort and reward varied across 5 levels, with each combination of reward level x shock level being presented 6 times in a semi-randomised order, totalling 150 runs.

Half of the runs (75) were directed at the participants (self-benefitting condition) and the other half at the confederate (prosocial condition). Target, effort level and reward level

were presented to the participants on a screen inside the scanner. The target of each run was indicated by either the name of the confederate, during the prosocial condition, or "You" (*Du*), during the self-benefitting condition, both written in the middle of the screen. The effort level was indicated via a 5-sliced cake diagram. Shock reduction was indicated by the total number of shocks displayed beneath the cake diagram. Participants were given 3 seconds in total to decide and were instructed to decide as quickly as possible (decision phase). After choosing either option, participants were presented with a virtual rectangle which filled up depending on the force with which they gripped the hand-dynamometer. For a successful run of the effort options, participants needed to fill up the rectangle above an indicator line and hold the applied force for one second, with a 3-second time limit to do so (effort phase). Failure to exert the required effort or to decide between the two options in the given time window resulted in 10 shocks being saved for the run. The effort phase was followed by a one-second feedback screen showing the number of shocks saved (feedback phase). Participants were specifically informed that for each run the resulting number of shocks would be saved based on their task performance, and 3 random runs would be selected for each target (self/other) from which the total number of shocks would be applied after the task. The whole task consisted of 6 trials á 25 runs with a pause between block 3 and 4 during which mood (PANAS) and sustained pain ratings were taken via a Visual Analogue Scale (VAS). Before the start of the task, participants were also given two practice runs. During the first practice, participants learnt to decide in the specified timeframe between two options. In the second practice run, participants learnt to gauge how much effort is connected to each effort level visualised.

Figure 3

Prosocial Effort Task Procedure



Note: Exemplary procedure of a prosocial effort task run. Only prosocial choices were analysed in this thesis.

fMRI-Image Acquisition

Functional imaging data were acquired using a T2*-weighted echo-planar imaging (EPI) sequence sensitive to blood oxygen level–dependent (BOLD) contrast using a SIEMENS 3 TESLA MRI scanner. Each volume consisted of 91 axial slices (voxel size: 2x2x2 mm; slice gap = 0.4 mm; TE = echotimes = 34 ms; flip angle = 66°) acquired with a repetition time (RT) of 1.2 s. The number of slices per volume (91) and reference slice (46) were defined according to the scanner acquisition order. High-resolution T1-weighted anatomical images were additionally collected for normalisation and anatomical localisation.

Analysis

Behavioural Analysis

All behavioural analyses were conducted in *RStudio* (RStudio Team, 2025) using the *lme4* (v1.1-26; Bates et al., 2015) package. To investigate the behavioural hypotheses, linear mixed-effects modelling (LMM) was implemented. Since only data of the experimental group was included in the analysis, the chosen methods were based on analysing a repeated-measures design. LMMs allow modelling of both fixed effects and random effects simultaneously, which is well suited for data in which both between-subject and within-subject variation is expected. Further fixed-effect models are extremely robust to violations of distribution assumptions (Schielzeth et al., 2020). The model estimates were calculated using restricted maximum likelihood (ReML) which is the default estimation method employed by the lme() function. Model assumptions (linearity, homoscedasticity, and normality of residuals) were checked using the *Dharma* package (Hartig, 2022) (for a detailed description see Appendix E). For all models a significance threshold of $p \leq 0,05$ was implemented.

Quality Checks

For general quality checks the data were inspected for completeness as well as plausibility. Participants were excluded if they didn't complete more than one whole block of the prosocial effort task (<125 trials) (3 participants) or didn't answer at least two of the three pain intensity VAS of interest (VAS 3, 4, 5) (2 participants). One participant was excluded because they only chose the effort option throughout the entire task, indicating a faulty MVC calibration. One additional participant was excluded because they never chose the prosocial option during the prosocial effort task. Further, two participants were excluded because they didn't experience sufficient sustained pain after the application of the pain cream (mean VAS ratings < 2).

Manipulation Checks

To assess if participants engaged in the prosocial effort task as intended, all participants were asked to fill out a post-experiment questionnaire concerning confederate deception, strategy use, and task comprehension as well as other general questions (see Appendix E). Participants were excluded if they reported not believing the confederate deception and changing their behaviour based on these doubts (e.g., "I thought the other person wasn't actually participating in the experiment"). Three participants shared minor doubts of the deception (e.g., "I wasn't sure if the other person was a psychology student");

however, on observation of choice behaviour, no inconsistencies from the rest of the sample were found. Further, if participants reported a fundamental misunderstanding of the experimental procedure (e.g. “Since I didn’t receive a painful stimulus during the task, I thought no painful stimuli would be applied”), their performance during the task would be checked for inconsistencies. Finally, if participants reported using a strategy which would hinder interpretation of the outcome (e.g., “I only chose the effort option every third time”), their data would be analysed for unusual task behaviour. Checking the data would, for example, include looking at the relationship between choices and effort reward, which is expected to be approximately linear (higher effort → fewer effort choices; higher reward → more effort choices). However, different aspects of task performance would be checked based on the post-task questionnaire answers. No participants were excluded based on the aforementioned manipulation checks. All following analyses were conducted with a data set consisting of the 30 remaining participants.

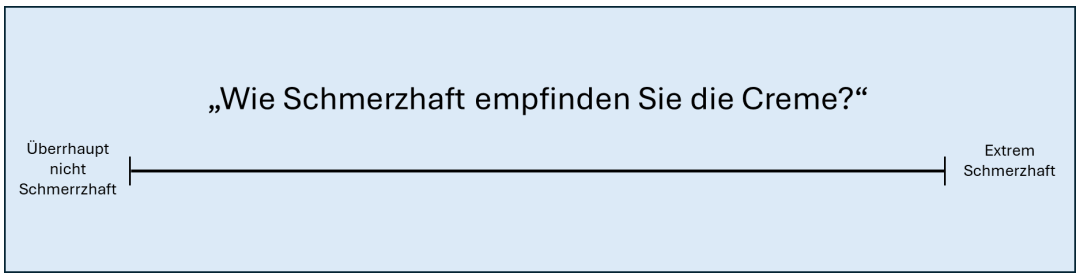
Behavioural Variables

VAS Pain Measure

Throughout the experiment, participants were also repeatedly (5 times) asked to answer the German version of the Positive and Negative Affect Schedule (PANAS, Krone et al., 1996) and rate their pain intensity on a visual analogue scale (VAS, 4 times) (see figures 2 & 4). Pain intensity ratings always consisted of a 9-point VAS scale (0 = "not painful at all”, 8 = “extremely painful”) as well as a question displayed above the scale. Participants used an MRI-safe button box to navigate the VAS and log in their answer. The VAS pain intensity ratings served the purpose of being the main pain perception measure of the experiment and consisted of one question on the pain intensity of the pain cream: "How painful do you perceive the heat cream?” (“Wie schmerzhaft empfinden Sie die Crème?”). To rate the pain intensity, participants freely mark a point between minimum and maximum. Participants were instructed to answer as quickly as possible and log in the first reaction to minimise strategic reporting and conserve the affective experience.

Figure 4

VAS Pain Intensity Measure



Note: To rate ongoing pain intensity, participants were asked to use a VAS. Participants could navigate the VAS with either the arrow buttons on a keyboard (outside the scanner) or with a button box (inside the scanner).

Sustained Pain Ratings (SPR)

To assess changes in pain perception of the applied pain cream, participants were asked to report pain intensity at specific timepoints throughout the experiment via VAS pain ratings. For this analysis ratings of VAS 2, VAS 3 and VAS 4 were used as the primary measurement of pain intensity. VAS 2 was presented before the prosocial effort task and was used as a baseline assessment of pain intensity before any prosocial behaviour was performed (baseline pain ratings) and was used to control for sensitivity differences to the effect of the pain cream. VAS 3 and 4 were used as during- and post-task pain measurements, respectively. VAS 3 was included to analyse the effect of intraindividual differences of the predictors on the sustained pain report, as well as to not further reduce the number of data points available.

Pain Ratings Difference Index (PDI)

To analyse the effect of non-task-related measures on pain changes during the task, a simple difference index was created. This pain difference index (PDI) was calculated using the difference of the pain ratings before and after the prosocial effort task (VAS 2 – VAS 4) of each participant. A positive value indicated the pain ratings were higher after the task, while a negative value indicated a reduction in pain ratings.

Prosocial Choice Sum (PC)

To investigate how the number of prosocial choices, in other words the general prosociality, affect SPR, the sum of prosocial choices was calculated for each participant and the subsequent VAS. PC represents the total number of prosocial effort choices (choosing the

effort option during the prosocial condition of the prosocial effort task) each participant made before the subsequent pain ratings (runs 1 - 3 for VAS 3 & runs 4 – 6 for VAS 4).

Prosocial Effort Index (PE)

To assess how prosocial effort investment influenced SPR, a prosocial effort index (PE) was calculated for each participant using data from the prosocial effort task. The required effort level was coded numerically in the data corresponding to a set proportion of the participants' MVC (1 = 40%, 2 = 50%, 3 = 60%, 4 = 70%, 5 = 80%). Since SPR and required effort level measurements differed in granularity (prosocial effort was measured on a trial level; SPR on a timepoint level), the index was created by calculating the means of the required effort level of prosocial effort choices for each subsequent timepoint per participant. This means that the PE for VAS 3 consisted of the mean effort level of runs 1 to 3, and the PE for VAS 4 consisted of the mean effort level of runs 4 to 6 of the prosocial effort task (e.g., a value of PE = 4.34 for VAS 4 → The participant's choice of the prosocial effort option had an average effort level of 4.34 during runs 4 to 6).

Prosocial Reward Index (PR)

The same procedure used to calculate PE was again implemented to calculate a prosocial reward index using the mean reward level for each prosocial choice per VAS and participant. The raw reward level was similarly coded to numerically represent a set reduction in shocks compared to the no-effort option (1 = 5 shocks, 2 = 4 shocks, 3 = 3 shocks, 4 = 2 shocks, 5 = 1 shock).

Behavioural Model

To investigate Hypotheses 1a, 1b and 1c, an LMM was constructed using PE, PR, and PC as fixed effects and the time points (VAS 2, 3 & 4) as a covariate to control time effects. The VAS sustained pain ratings 2-4 were used as the dependent variable and subject ID as the random effect (*Pain ~ Timpoints + PE + PR + PC + (1|ID)).* Meaning, every participant had their own intercept, which helped to control for baseline pain sensitivity.

fMRI Analysis

First-Level Analysis

For the first-level analysis, all fMRI data were preprocessed and analysed using *SPM12* (Wellcome Trust Centre for Neuroimaging, London, UK) as well as *Nipype* (Gorgolewski et al., 2011) implemented in *MATLAB* (The MathWorks, Natick, MA, USA).

Statistical analyses were conducted within the general linear model (GLM) framework as implemented in *SPM12*. The model specification included all experimental

conditions of interest: *decision_self*, *decision_other*, *effort_self*, *effort_other*, *feedback_self*, and *feedback_other*. For each condition, onset times and durations were extracted from subject-specific event files. Conditions were modelled using the canonical haemodynamic response function (HRF) without temporal or dispersion derivatives. Functional images were modelled in seconds, with a repetition time (RT) of 1.2 seconds. Events were modelled as stick functions since the experimental design used discrete, temporally separated task events. High-pass filtering (cutoff = 128 s) was used to remove low-frequency drifts. No factorial design structure was defined. Global normalisation was disabled, and an implicit mask was applied, excluding voxels below 80% of the global mean signal intensity. Serial correlations in the time series were modelled using a first-order autoregressive model to account for temporal autocorrelation in BOLD data. No explicit masking image was provided. Motion parameters derived from realignment were included as regressors of no interest for each run. Model parameters were estimated using restricted maximum likelihood (ReML) estimation.

All analyses were performed on preprocessed T2-weighted functional images; high-resolution T1-weighted anatomical images were used exclusively for co-registration and normalisation to standard MNI space.

Second-Level-ROI-Analysis

All second-level analyses were performed in *Python 3.11* (Python Software Foundation, 2023) using the *Nilearn* toolbox for functional neuroimaging (Abraham et al., 2014; Nilearn Developers, 2024). Code was developed and executed in the *Spyder IDE* (Raybaut & The Spyder Project Contributors, 2024). General linear modelling, mixed-effects modelling and false discovery rate (FDR) correction, in the form of the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995) to correct for multiple comparisons, was done using the *statsmodels* package (Seabold & Perktold, 2010). The regions of interest (ROI) consisted of the ventromedial prefrontal cortex (vmPFC), connected to valuation and meaning (Bartra et al., 2013), as well as altruistic analgesia, transforming meaning-related valuation processes into modulation of pain perception (Roy et al., 2009; Sola et al., 2019; Wang et al., 2020); the anterior cingulate cortex (aCC) and the anterior insula (AI), both indicated to play vital roles in affective pain experience (Atlas, 2021; Krueger et al., 2020; Labrakakis, 2023; Lançon & Séguéla, 2023; Wager et al., 2016); and the primary somatosensory (S1) cortex, widely associated with the sensory pain experience (Rainville, 2002; Sun et al., 2023).

Since the findings by Wang et al. (2020) are the main source for the neuromodulatory processes connected to altruistic analgesia, all coordinates were taken from their paper (see Table 2). The vmPFC coordinates were based on the peak activation during donating (donation stage), while activation of all other ROIs was defined by the peak activation during the pain application (pain stage) of their second experiment (since only pain-related activation is relevant for the analysis). For all ROIs a 4 mm sphere was defined surrounding the specified coordinates, with all voxels inside the sphere (voxels with their centre inside the sphere) representing the ROI.

Table 2

MNI-Coordinates of the ROI

Regions	x	y	z
vmPFC	0	56	-4
Left AI	-36	-2	14
Right AI	-36	-16	2
aCC	-8	44	4
Left S1	-28	-32	60
Right S1	28	-32	60

vmPFC-PDI Model

To investigate Hypothesis 2a, the beta-weight maps of the decision and feedback phases were extracted for each subject and subsequently averaged across runs and conditions within each participant. Mean voxel-wise activation values were then computed within the predefined vmPFC ROI. The effort phase was not included in this analysis since data are more likely to be confounded by movement (Mazaika, Whitfield-Gabrieli, & Reiss, 2007). Based on this reasoning, a general linear model (GLM) was constructed. This model consisted of vmPFC activation based on beta-weight maps using the aforementioned process. The dependent variable consisted of each participant's PDI (PDI ~ vmPFC).

vmPFC cross-regional Covariation Models

To investigate Hypotheses 2b & 2c, the beta weight maps of all ROIs (vmPFC, AI, aCC, & S1) were extracted for each subject. For this analysis, the beta-weights were not averaged however to preserve the temporal structure of the data and increase sensitivity to coactivation. While the relationship between neural activation and pain report is based on two measures taken at separate times, it is possible to look at the relation of vmPFC activation

with activation in other brain areas connected to pain simultaneously. Additionally, the vmPFC activation was mean-centered. As mentioned in the introduction, there is little research on how meaning-related vmPFC activation differs during prosocial decision-making (decision phase) vs experiencing the outcome (feedback phase), so there is not enough evidence to form a conclusive hypothesis. However, since vmPFC activation does seem to differ between phases (Vassena et al., 2014), excluding the condition from the model would reduce power, influence residual power and force the model to treat phase variance as noise (Gueorguieva & Krystal, 2004). Using these variables, three LMMs were constructed, one for each pain-related ROI (AI, aCC and S1) with the vmPFC activation and phase interaction being the predictors for all models, with subject ID being the random effect (ROI ~ vmPFC*Phase). For simplification, the activation of hemispherical brain areas was combined into a single activation variable by using the mean activation of both hemispheres. FDR correction was used to correct for multiple comparisons.

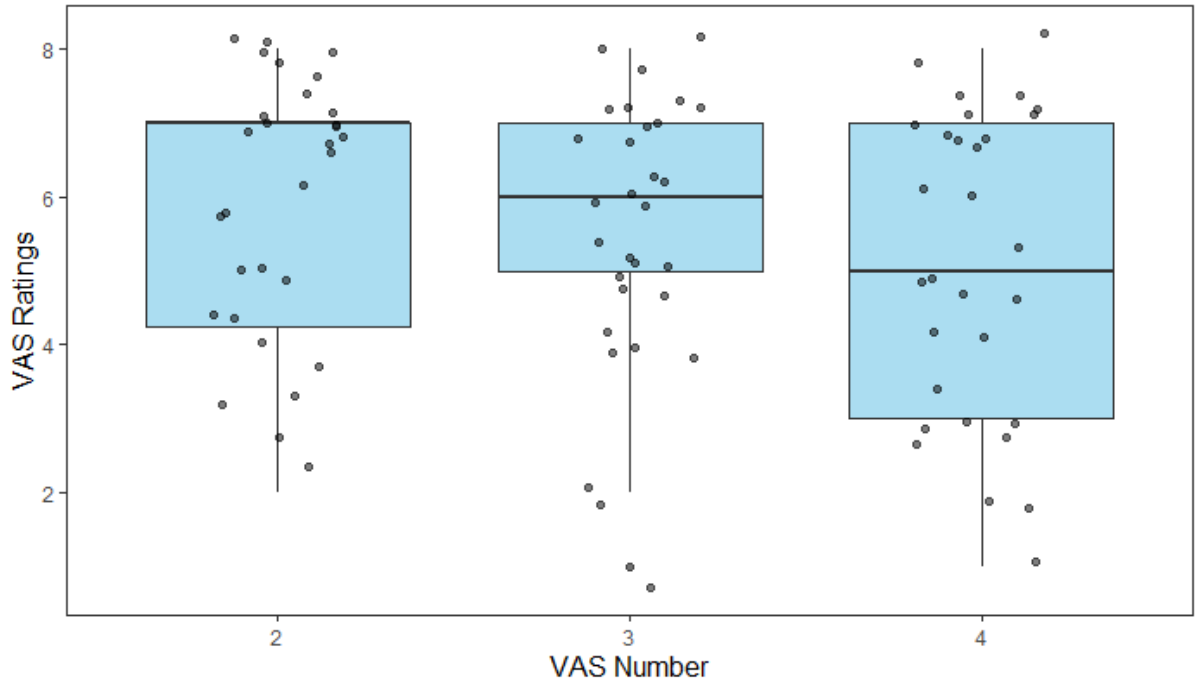
Descriptive Analysis

Pain Ratings

Throughout the three timepoints examined (VAS 2-4) in this analysis, participants reported on average moderate VAS-pain ratings (M = 5.442) with a wide variance ($Range_{SDR}$ = 1:8, SD_{SDR} = 1.905, IDQ_{SDR} = 3) within as well as between subjects. Over the three timepoints, general pain ratings trended downwards, although not significantly (see Figure 5 & Figure F1)

Figure 5

Pain Ratings Across Timpoints



Note: Boxplot visualizing the participants VAS pain ratings across measurement timepoints.

Effort-Task Indices

Participants tended on average to choose prosocial effort options with similar effort requirements (M_{PE} = 3.011, SD_{PE} = 0.163, $Range_{PE}$ = 2.825:3.333, IDQ_{PE} = 0.320). The same lack of between- as well as within-person variance can also be observed when looking at the mean prosocial reward level (M_{PR} = 3.005, SD_{PR} = 0.09779475, $Range_{PR}$ = 2.875:3.142, IDQ_{PR} = 0.160). Some of the lack of variance can be attributed to the aggravated nature of the variables. However, most can be explained by a lack of inter- as well as intra-individual variability of behaviour throughout the task, since raw task data reflect the tendency for low-effort, high-reward choices (see Figure F2a-b). Further, PE and PR are exhibiting a semi-bimodal distribution around the mean (see Figure F3a-c). However, since the general variance of the distribution is so low, observed maxima and minima are still close to the mean compared to the possible maxima and minima of the measure. Prosocial choice behaviour during the

prosocial effort task was, on the other hand, exhibited in a comparably higher amount of variance (M_{PC} = 36.906, SD_{PC} = 3.032, $Range_{PC}$ = 24:40, IDQ_{PC} = 1).

Results

Behavioural Hypotheses

Behavioural Model

As shown in Table 3 and Figure 5, none of the fixed effects were significant (Rmarg = 0.03), while most of the variance of SPR was explained by individual differences (Rcond = 0.62). The effect of time was statistically non-significant (beta = -0.37, 95% CI [-1.01, 0.28], t(83) = -1.13, p = 0.262; Std. beta = -0.16, 95% CI [-0.44, 0.12]). The effect of PR was statistically non-significant (beta = -0.41, 95% CI [-7.69, 6.87], t(83) = -0.11, p = 0.912; std. beta = -0.31, 95% CI [-5.80, 5.18]). The effect of PE is statistically non-significant (beta = 0.15, 95% CI [-5.82, 6.12], t(83) = 0.05, p = 0.961; std. beta = 0.11, 95% CI [-4.42, 4.64]). The effect of PC other is statistically non-significant (beta = 0.02, 95% CI [-0.11, 0.15], t(83) = 0.31, p = 0.759; std. beta = 0.19, 95% CI [-1.01, 1.38]).

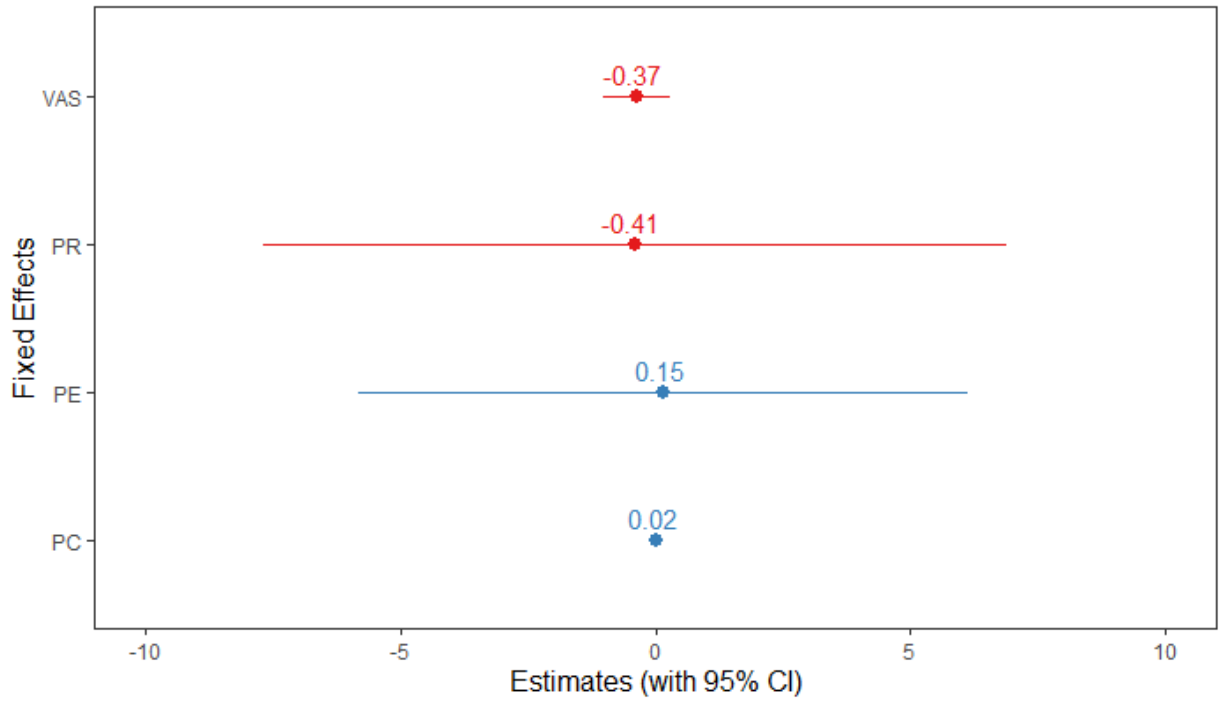
Table 3

Behavioural Model Estimates

Fixed Effects	Estimate	Std. Err	df	t	P	95% CI
Intercept	6.667	0.732	74.912	9.096	9.86e-14	5.21, 8.13
VAS	-0.366	0.323	56.38506	-1.134	0.262	-1.01, 0.28
PR	-0.408	3.659	58.41919	-0.112	0.912	-7.69, 6.87
PE	0.147	3.002	57.63141	0.049	0.961	-5.82, 6.12
PC	0.019	0.064	61.36110	0.308	0.759	-0.11, 0.15

Figure 6

Behavioural Model Estimates



Neuronal Hypotheses

vmPFC-PDI-Model

Using a GLM, I found no significant effect of averaged beta-weight maps in the ROI on PDI, indicating no effect of vmPFC activity during the prosocial decision and feedback phase of the prosocial effort task on pain change and, consequently, no indication that vmPFC activation was connected to an analgesic effect (see Table 4).

Table 4

vmPFC-PDI-Model Estimates

Predictors	Estimate	Std.Err.	z	P	95% CI
Const	-0.7625	0.6657	-1.1454	0.2521	-2.0672 - 0.5423
vmPFC	0.0701	0.3726	0.1880	0.8509	-0.6602 - 0.8003

vmPFC Cross-Regional Covariation Model

As shown in Tables 4a, b & c, all three LMMs show a significant positive covariation between vmPFC activation and activation in the respective pain-related ROI. Further, there is a significant negative interaction between Phase and the vmPFC slope in all models. Since our phase baseline is the decision phase, this means that the positive covariation is

significantly higher during the decision phase. However, the covariation remains positive across phases.

Table 5a

AI Model Estimates

Fixed Effects	Estimate	Std.Err.	z	P	P_{FDR}	95% CI
Intercept	0.409	0.230	1.780	0.075		-0.041, 0.860
Phase [feedback]	-1.436	0.276	-5.202	<0.001	<0.001	-1.977, -0.895
vmPFC	0.742	0.008	97.002	<0.001	<0.001	0.727, 0.757
vmPFC:Phase [feedback]	-0.534	0.037	-14.340	<0.001	<0.001	-0.607, -0.461

Note: Results of the LMM using AI activation as dependent variable with FDR-corrected p-values ($P_{FDR)}$

Table 5b

S1 Model Estimates

Fixed Effects	Estimate	Std.Err.	z	P	P_{FDR}	95% CI
Intercept	-0.246	0.338	-0.729	0.466		-0.909, 0.416
Phase [feedback]	-1.977	0.364	-5.439	<0.001	<0.001	-2.690, -1.265
vmPFC	0.933	0.010	92.151	<0.001	<0.001	0.913, 0.953
vmPFC:Phase [feedback]	-0.651	0.050	-12.970	<0.001	<0.001	-0.749, -0.553

Note: Results of the LMM using S1 activation as dependent variable with FDR-corrected p-values (P_{FDR})

Table 5c

aCC Model Estimates

Fixed Effects	Estimate	Std.Err.	z	P	P_{FDR}	95% CI
Intercept	-0.105	0.202	-0.521	0.603		-0.501, 0.291
Phase [feedback]	-0.550	0.255	-2.162	0.031	<0.001	-1.049, -0.052
vmPFC	0.800	0.007	113.922	0.000	<0.001	0.787, 0.814
vmPFC:Phase [feedback]	-0.503	0.034	-14.692	0.000	<0.001	-0.570 -0.436

Note: Results of the LMM using aCC activation as dependent variable with FDR-corrected p-values (P_{FDR}).

Discussion

In this master's thesis I investigated the effect of prosocial choice, level of invested prosocial effort and level of prosocial reward on sustained acute pain. Further, I investigated vmPFC activation during a prosocial effort task and its connection to pain intensity reports and activity in pain-related brain areas. On a behavioural level I found no significant effect of any of the indices related to prosocial behaviour (Hypotheses 1a, b & c). Indicating that neither prosocial effort level, prosocial reward magnitude nor the number of prosocial choices had any significant effect on sustained pain ratings. Further, I found no connection between vmPFC activation during prosocial choice and feedback and a pain difference score (Hypothesis 2a). Similarly, I found no negative covariation between vmPFC activity and pain-related areas (Hypothesis 2b & c).

Before discussing my findings in the context of prior literature, some inherent limitations of using data from a study not designed for the research question investigated in this master's thesis need to be discussed. The most immediately impactful limitation is the reduced sample size. Since the larger research project was not built around my research question, I could not determine an adequate sample size using a priori power analysis. Furthermore, since I could only use one half of the whole sample (experimental group), I was generally left with a fairly small sample for the type of analysis and the nature of the data present. This very likely led to all analyses being significantly underpowered. Consequently, even if generally there would have been an effect present, the analysis would have had a small probability of detecting it.

Moreover, the general study design of the larger research project was not optimal for my research question. While a repeated-measures design is an adequate approach to investigate the influence of interventions on a painful stimulus, the nature of the task led to a lack of variance exhibited by the main predictors (see Descriptive Analysis). This leads to three main considerations for model performance and interpretation. Low variation of the predictor can inflate type-II errors, leading to increased confidence intervals and non-significant estimates even if there is a theoretical relationship. Further, the explanatory power of a model tends to be very low since the variance of the outcome cannot be explained by variation in predictors if there is little variance. Additionally, it can also lead to inflated multicollinearity since low variance in predictors can also lead to small variance between predictors. Combined with the rather small sample size, these limitations may lead to an unstable and very much underpowered model, which might explain the lack of significance of the predictors and explanatory power of models using data from the prosocial effort task.

Further, since the pain measure was not designed to be the main outcome variable, there are some further limitations that must be considered. In the overarching study design, the pain measure mainly served the purpose of making sure that participants were actually in pain as well as to account for between-subject differences in reactions to the heat cream. Consequently, the pain measure was rather infrequent (once every 75 trials of the prosocial effort task). More frequent measurements might give a better understanding of how the pain experience evolves over time and might uncover more short-lived effects in pain modulation, which might arise when the pain measure is more precisely matched with the prosocial behaviour. Utilising a between-group design enforcing differences in prosocial choice, effort and reward by having the control group perform a similar task without the prosocial context and comparing pain ratings between groups could circumvent some of these issues. Another way to possibly increase variance in predictors would be to increase granularity of the pain ratings to a trial level, making it possible to preserve trial-level variance of predictors and additionally making it possible to analyse trial-level influence of predictors on pain ratings. Further, the implementation of more sensitive analytical approaches like Bayesian modelling might lead to a better representation of intricate relationships even if variance in behaviour is low.

Finally, the pain measure used in this study only consisted of a singular question and might have been unable to capture the complexity of the pain experience and thus given a less nuanced look at the influence of the prosocial effort on pain. For example, Lopéz-Sola et al. (2018) found that receiving pain as a prosocial act reduced pain-related unpleasantness, not the intensity of pain. Likewise, Ziida et al. (2024) found that pain modulation driven by emotional valence primarily affected unpleasantness ratings, similar to findings that empathy for pain mainly involves the affective but not the somatosensory aspects of pain (Singer et al., 2004). On the other hand, recent research on the effect of partner support on pain perception indicates that social affective input can indeed also reduce pain intensity ratings (Mazza et al., 2023), pointing towards a complex relationship between social/affective input and pain modulation, which is still not entirely understood. Conversely, the emotional/affective component has been shown to play a large part in pain modulation through social actions, so including a more diverse array of pain measures, especially when it comes to the emotional/affective component of pain, could have shed light on a more complex relationship between pain and social behaviour in general. Keeping these limitations in mind, other possible factors that led to the observed results are now discussed.

First, while Wang et al. (2020) investigated various different subtypes of prosocial behaviour, all of which led to reduced pain ratings, they did not look at helping behaviour associated with directly avoiding pain for others. As discussed in the introduction, pain avoidance has been suggested to modulate affective responses during prosocial behaviour differently to monetary reward (Crockett et al., 2014; Lengersdorff et al., 2020). On the one hand, this should induce higher meaning-related activity, heightening the analgesic effect compared to non-pain-related prosocial behaviour. On the other hand, the raised "stakes" of possible harm to another person might also induce a stress reaction.

Stress has been indicated to increase the perception of pain and negative affective states (Crettaz et al., 2013; Löffler et al., 2022), which could in turn confound the positive effect of the prosocial behaviour itself. However, it might also be possible that the "stakes" in the prosocial effort task were not high enough. While participants' behaviour could lead to a reduction in possible painful stimuli for the other person, pain could not actually be wholly avoided, which could have led to a reduction in meaning allocated to the behaviour. Furthermore, participants could only control the pain outcome for the other person to a certain extent, since the painful stimuli which would supposedly be applied after the task were randomly selected out of a great number of different decisions made by participants. While the prosocial effort task used in this study featured outcome feedback of the prosocial action, the actual meaningful consequences (administration of pain stimuli) were indirect and seemingly random. This could have again lessened the feeling of meaning ascribed to the prosocial action itself and in turn reduced the analgesic effect, since feelings of control have been shown to influence task valuation (Harmon-Jones et al., 2024).

Another difference in this thesis compared to prior research is the introduction of the variability of outcomes. Not only did the prosocial effort task utilise different levels of prosocial reward (shock reduction), but participants could also fail at helping, worsening the outcome for the other person (a confederate). Failure feedback has been indicated to increase pain perception (van den Hout, 2000) and heighten stress as well as increase negative emotions (Jones et al., 2013). These effects could have negatively influenced the analgesic effect of the prosocial measures.

However, it is of note that the failure rate during the prosocial effort task was fairly low at 5.4% across all participants and runs, possibly mitigating such a negative impact. Further, the pain stimulus used in this study differed from painful stimuli used in prior literature. The pain cream used in this study induced sustained tonic pain, while most prior research focused on phasic, short-lived pain stimuli (Brown et al., 2003; López-Sola et al.,

2018 & 2019). While tonic pain has been shown to be more susceptible to analgesic effects (Olesen, 2014; Hummel et al., 1995), enduring pain over a long period can again induce stress and induce negative affect, which again mutually reinforce each other (Aboushaar & Serrano, 2024). This dynamic could have further confounded a possible analgesic effect of prosocial behaviour. It is of note that Wang et al. (2020) did observe an altruistic analgesic effect even in chronic pain patients (Experiment 3). However, chronic pain is often connected to dysfunctions in endogenous pain modulatory systems which could interact with this altruistic analgesia (Knauf & Koltyn, 2014; Nijs et al., 2012) and should not be present in healthy individuals and experimentally induced tonic pain.

Also, while there is evidence that generally effortful prosocial behaviour can have an analgesic effect (Wang et al., experiment 1 & 3), this thesis is the first to utilise a prosocial effort task based on physical effort to investigate altruistic analgesia, introducing physical exertion as a variable.

Prior research suggests that general physical exertion can affect pain perception (Lima et al., 2017). However, this connection of physical exertion and pain is not straightforward. Generally, dynamic resistance exercises, like the hand contraction used in the prosocial effort task, have been shown to induce hypoalgesia (reduction of pain sensitivity) even at low MVC values of 10-30% (Hoeger-Bemont et al., 2008). However, most studies investigating these hypoalgesic effects induced through exercise (EIH) did not induce the painful stimuli parallel to the exercise but rather before and after (Rice et al., 2019). The main research on how pain is influenced by exercise during pain are studies of EIH in chronic pain patients. This research has shown that exercise can even increase pain perception under certain circumstances (Meeus et al., 2010). While, of course, the tonic pain induced in this study cannot replicate side effects of conditions connected to fibromyalgia and chronic fatigue syndrome (both connected to chronic pain), these findings do indicate that sustained pain can interact with physical exercise, dampening a possible analgesic effect or even reversing it. Further, EIH is still not entirely understood (see Rice et al., 2019, for review), making inferences about the effects on less well-studied types of analgesia like altruistic analgesia difficult. In this study at least no EIH seems to have been present since PE showed no effect on pain perception, and it is possible that the effect of PE was influenced by the pain being parallel to the effort.

How exactly the experience of meaning influences pain perception is also still unclear. In this study the painful stimulus was disconnected from the prosocial behaviour itself, meaning that the endurance of pain was not directly connected to the prosocial

outcome. In the experiment by López-Solà et al. (2018), the endurance of the painful stimulus itself was the prosocial behaviour which López-Solà et al. (2018) propose changes the meaning of the pain itself and induces the analgesic effect, which should not be the case for pain, which is totally detached from the prosocial action. While Wang et al. (2020) did observe an analgesic effect in both pain-connected (pilot study 1) and detached (e.g., experiment 2) and even during sustained detached pain (experiment 3), all observations not only differed in the role of pain in the prosocial behaviour but also in the nature of the painful stimulus itself (mechanical, thermal, electrical, chronic, acute, etc.). So, while the effect of both analgesia connected as well as detached from pain seems to be meaning related, it is still not clear if and how pain modalities, such as quality and context connected to prosocial behaviour, influence the analgesic effect and its underlying neural substrate. The pain stimulus applied in this master's thesis was entirely detached from the prosocial action which again could have influenced the analgesic effect.

Since participants also engaged in self-benefitting behaviour during the prosocial effort task, it is further possible that model estimates were confounded by effects specific to self-benefitting actions. However, the aforementioned interaction with feedback, failure, etc. could have further led to unpredictable interactions.

In this study, I did not find a significant effect of vmPFC activation during prosocial choice or feedback on pain ratings. There are several plausible explanations for why vmPFC signals did not translate into measurable changes in pain perception here. One crucial point is that the vmPFC does not directly modulate pain intensity. Instead, it seems to be more involved in shaping expectations and updating contextual meaning. Motzkin et al. (2023) showed that people with vmPFC lesions had stronger cue-based expectancy effects on pain but no changes in their baseline sensitivity. This suggests that the vmPFC might contribute more to how we interpret pain, considering the specific context, rather than directly altering the sensory experience.

Moreover, the vmPFC's influence could target the affective dimension of pain to a higher degree than intensity. In this study only reports on pain intensity in the form of VAS ratings were collected, which could have decreased the observed effect. Nonetheless, it is of note that prior research did find an analgesic effect of prosocial behaviour, even when using only pain intensity ratings (Wang et al. 2020).

However, the LMMs analysing vmPFC activity with activation in areas related to the affective dimension of pain showed no indication of any type of downregulation of the affective component of pain. On the contrary, the model estimates indicate a high

coactivation between the vmPFC and the affective as well as somatosensory brain areas during prosocial choice and feedback, which indicates that vmPFC activity was associated with an increased activation in pain-related brain areas. While there was a significant interaction between the vmPFC slope and phase in all LMMs, the slope remained positive across phases, indicating that while the positive covariation during the prosocial effort task was lower during the feedback phase compared to the decision phase, the difference was not big enough to reverse the positive covariation. The usage of second-level beta estimates for the LMM does also not permit inference of connectivity, which makes claims about differences in connectivity based on the phase impossible. Consequently, due to the extent of the covariation contrary to prior findings, other possibilities have to be considered. One possible cause for this extremely positive covariation could be simple overfitting due to the small sample size.

While generally top-down pain modulation is connected to reduced activation in the AI and aCC (Atlas, 2021; Lançon & Séguéla, 2023) both areas are also indicated to play a role during decision-making and social cognition (Krueger et al., 2020, Lavin et al., 2013). Prior work shows that vmPFC and AI interact during prosocial decision-making to balance valuation of others' outcomes with the aversiveness of their suffering (Hiser & Koenigs, 2018). This means that the specific paradigm used in this master thesis (e.g. making decisions directly connected to the other person's suffering while knowing that the other person is also presented with choices, which directly influence one's own suffering as well as their own) could have complicated the extraction of AI activation specific to affective pain reaction. This again could have contributed to the positive covariation between vmPFC activation and AI activation being exaggerated and possibly hiding effects related to downregulation. Likewise, the aCC has been indicated to be involved in effort-based decision-making, conflict monitoring, and integration of cost-benefit signals, including in social and prosocial contexts (Klein-Flügge et al., 2016). So, while prosocial behaviour might act to downregulate the affective component of pain, the affective brain areas are also tightly interwoven with prosocial behaviour itself. This in turn could've played a role in overestimating the positive covariation of vmPFC and ACC activation.

Further, the vmPFC, as is the case with all defined brain areas, does not work in isolation. In Wang et al. (2020), prosocial acts reduced pain and pain-related brain activation, but the vmPFC's role was mediated through changes in the insula and aCC.
In other words, vmPFC valuation signals may need to interact with salience and affective pain networks in order to influence pain. Similarly, prior research on vmPFC-based pain

modulation emphasises its role as a hub connecting social input to brain regions more directly connected to pain perception (Sharvit & Schweinhardt, 2022). These complex connections could possibly be harder to quantify using a beta-coefficient-based LMM, which in part could have been a driving factor of the high positive covariation of activation during the prosocial effort task.

Finally, there are some practical considerations. The vmPFC is particularly difficult to image reliably with fMRI due to its susceptibility to artefacts (its proximity to the orbital sinuses causes signal dropout and distortion) (Chang et al., 2021), so ROI averages may wash out subtle effects. The behavioural pain measures were also fairly coarse (a limited number of VAS ratings), meaning that small neural modulations could easily go undetected.

Outlook

While this master´s thesis tried to investigate the influence of different qualities of prosocial behaviour like prosocial choice quantity, effort investment, and quantitative variation in outcome, exploring a wider variety of distinct factors might have facilitated more nuanced interpretations. This widening of the research focus would benefit from a more controlled introduction of varied factors which might influence the analgesic effect. For example, future research could vary the level of control over the outcome, possibility of failure/failure rate and outcome salience between experimental/control groups, making isolation of unique effects of the aforementioned factors easier compared to the repeated-measures design utilised in this thesis. Similarly, while prior research has investigated this altruistic analgesia using a variety of different pain stimuli, prosocial behaviours and contexts, this variation has never been controlled to a degree where inferences of individual influence could be made. Conducting a larger research project with controlled variations in experimental design (e.g., attached vs detached pain, tonic vs acute pain, donating vs pain reduction) could lead to a better understanding of the actual mechanics behind this analgesia and how these variables influence top-down pain modulation.

Furthermore, while fMRI analysis holds information concerning general brain activity, the biochemical/neurochemical pathways (endorphins, oxytocin, dopamine, etc.) that mediate the pain reduction from altruism are less well mapped. For example, another possible mechanism may be that pain modulation is driven by the intrinsic reward of prosocial behaviour itself through dopamine, which has been suggested in reward-based pain reduction (Wang et al., 2021; Wood, 2008). However, research on the role of dopamine in prosocial reward has been contradictory, with some studies suggesting a direct role of the mesolimbic

pathway in prosocial reward as well as self-benefitting reward (Harbaugh, Mayr, & Burghart, 2007; Lewis et al., 2021; Walsh et al., 2021), while other studies suggest the mesolimbic pathway to be uniquely activated by self-benefitting behaviour in contrast to prosocial behaviour (Lockwood et al., 2022). Future research could directly look at dopamine levels and activity in the mesolimbic dopamine pathway during prosocial behaviour to investigate differences in reward processing in various prosocial behaviours and reward types. Likewise, oxytocin has been shown to influence pain perception (Kawasaki et al., 2024) and to play a complex role in empathetic responses (Barraza & Zak, 2009) as well as prosocial behaviour (Mobbs et al., 2009). Investigating the possible role of oxytocin as a mediator of the proposed altruistic analgesia in future research could uncover interesting new interpretations of the interplay of prosocial behaviour and pain perception.

Concluding Remarks

With consideration of the aforementioned limitations, I found no evidence that prosocial effort to avoid the pain of strangers induces a reduction in the perception of sustained pain. Further, I found no evidence that vmPFC activation during prosocial behaviour affects pain perception. Considering the prior research does indeed suggest a general analgesic effect of prosocial behaviour, these findings indicate that the connection between prosocial behaviour, valuation and pain perception could be more intricate than expected. This makes further research of the phenomenon even more important since understanding how pain can be influenced by social cognition and behaviour holds interesting implications not only for therapeutic use but also for the general mechanism behind pain perception.

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Appendix A

Abstract

Recent research indicates that prosocial behaviour can directly influence the prosocial actors' pain experience. While not yet entirely understood, this analgesia seems to be driven by

processes related to the experience of meaning as well as a downregulation of pain-related areas through the ventromedial prefrontal cortex (vmPFC). Using repeated-measures behavioural as well as functional magnetic resonance imaging (fMRI) data from a larger research project, this master's thesis aimed to investigate how variations in effort, outcome, and choice behaviour as well as vmPFC activation influenced this proposed analgesic effect. Further, this master's thesis examined the role of the vmPFC as a proposed hub between social input and neuronal pain modulation. Specifically, linear mixed modelling and general linear modelling paradigms were implemented to investigate how task performance and vmPFC activation during a prosocial effort task influenced pain intensity ratings and neural activity in pain-related brain areas. However, no significant effect of any prosocial behaviour measures or vmPFC activation on pain reports or affective or sensory neural activation was found in the examined sample.
Keywords: prosocial behaviour, pain, vmPFC, AI, aCC, S1, effort, meaning

Zusammenfassung

Jüngste Forschungsergebnisse deuten darauf hin, dass prosoziales Verhalten die Schmerzwahrnehmung der prosozial-handelnden Personen direkt beeinflussen kann. Obwohl die genauen Mechanismen noch nicht vollständig verstanden sind, scheint diese schmerzlindernde Wirkung durch Prozesse im Zusammenhang mit dem Empfinden von Sinn, sowie durch eine Herunterregulierung schmerzbezogener Areale über den ventromedialen präfrontalen Kortex (vmPFC) bedingt zu sein. Diese Masterarbeit untersuchte anhand von wiederholten Verhaltensmessungen und funktionellen Magnetresonanztomographie-Daten (fMRT) aus einem grösseren Forschungsprojekt, wie Variationen in Anstrengung und Ergebnis sowie Aktivierung des vmPFC diesen vermuteten schmerzlindernden Effekt beeinflussen. Darüber hinaus untersuchte diese Masterarbeit die Rolle des vmPFC als mögliche Schaltstelle zwischen sozialer Interaktion und neuronaler Schmerzmodulation. Konkret wurden lineare gemischte Modelle und allgemeine lineare Modelle eingesetzt, um zu untersuchen, wie das Verhalten und die vmPFC-Aktivität während einer prosozialen Anstrengungsaufgabe die Schmerzwahrnehmung sowie die neuronale Aktivität von Schmerzarealen beeinflusst. Es zeigte sich jedoch kein signifikanter Effekt von prosozialen Verhaltensmaßen oder der vmPFC-Aktivierung auf die Schmerzberichte oder die affektive bzw. sensorische neuronale Aktivierung in der untersuchten Stichprobe.
Schlüsselwörter: Prosoziales Verhalten, Schmerz, vmPFC, AI, aCC, S1, Anstrengung, Sinn

Appendix B

Probandeninformation und Einwilligungserklärung zur Teilnahme an der Studie

„Auswirkungen von Schmerzen auf Soziale Wahrnehmung“

Sehr geehrter Teilnehmer, sehr geehrte Teilnehmerin!

Wir laden Sie ein an der oben genannten Studie teilzunehmen. Die Aufklärung darüber erfolgt über diese Probandeninformation und in einem ausführlichen Gespräch zu Beginn des Experiments, währenddessen Sie die Möglichkeit haben werden, Fragen zu den Inhalten der Studie zu stellen.

Ihre Teilnahme an dieser Studie erfolgt freiwillig. Sie können jederzeit ohne Angabe von Gründen aus der Studie ausscheiden. Die Ablehnung der Teilnahme oder ein vorzeitiges Ausscheiden aus dieser Studie haben keine nachteiligen Folgen für Sie.

Experimentelle Studien sind notwendig, um verlässliche neue Forschungsergebnisse zu gewinnen. Unverzichtbare Voraussetzung für die Durchführung einer Studie ist jedoch, dass Sie Ihr Einverständnis zur Teilnahme an dieser Studie schriftlich erklären. Bitte lesen Sie den folgenden Text als Ergänzung zum Informationsgespräch mit dem Studienleiter sorgfältig durch und zögern Sie nicht Fragen zu stellen.

Bitte unterschreiben Sie die Einwilligungserklärung nur

- wenn Sie Art und Ablauf der Studie vollständig verstanden haben,
- wenn Sie bereit sind, der Teilnahme zuzustimmen und
- wenn Sie sich über Ihre Rechte als TeilnehmerIn an dieser Studie im Klaren sind.

Zu dieser Studie, sowie zur Probandeninformation und Einwilligungserklärung wurde von der zuständigen Ethikkommission eine befürwortende Stellungnahme abgegeben.

1. Was ist der Zweck der Studie?

Der Zweck dieser Studie ist es, die Auswirkung anhaltender Schmerzen auf die Wahrnehmung des Schmerzes einer anderen Person zu untersuchen. Die zu diesem Zweck erhobenen Fragebogendaten, sowie Ihr Verhalten bei verschiedenen Experimentalaufgaben lassen Rückschlüsse darauf zu. Währenddessen wird zudem Ihre Gehirnaktivität mittels funktioneller Magnetresonanztomographie (fMRT) aufgezeichnet. Diese Methode erlaubt die Messung der Stoffwechselaktivität des

Gehirns, wonach Rückschlüsse über die Aktivität verschiedener Hirnregionen während der Experimentalaufgaben möglich sind. Nach erfolgter Studienteilnahme können Sie genauere Informationen zum Studienzweck erhalten. Dies dient dazu, möglichst natürliches Verhalten zu messen, da das Wissen um die genaue Forschungsfrage/den Studienzweck zu einer unbewussten Beeinflussung des Verhaltens der VersuchsteilnehmerInnen führen könnte.

2. Wie läuft die Studie ab?

Diese Studie wird von ForscherInnen der Universität Wien in Kollaboration mit der MedUni Wien durchgeführt und wird am Neuroimaging Center der Universität Wien (Standort Universitätszahnklinik, Sensengasse 2A, 1090 Wien) stattfinden. Es werden insgesamt 72 Personen im Alter von **18 bis 40** Jahren daran teilnehmen.

Ablauf der Untersuchungen

Vor dem Testtermin

Um zu erfahren, ob Sie als TeilnehmerIn für diese Studie geeignet sind, sowie um sicherzustellen, dass eine Teilnahme an dieser Studie keine Risiken birgt, ist es notwendig, dass im Vorhinein ein online Screening-Fragebogen vollständig ausgefüllt wird. Die Beantwortung dieses Fragebogens ist an keinen Ort gebunden, Sie benötigen lediglich eine stabile Internetverbindung. Zur besseren Lesbarkeit wird eine Bearbeitung des Screening-Fragebogens an einem Computer empfohlen. In diesem Fragebogen werden die Ausschlusskriterien und Sicherheitsfragen für Untersuchungen mit Magnetresonanztomografie abgefragt. Bevor Sie mit der Bearbeitung des Screening-Fragebogens beginnen, ist es notwendig, dass Sie die Teilnehmerinformationen ausführlich durchgelesen haben. Sie werden gebeten Ihr Einverständnis zur Studienteilnahme durch das Klicken des entsprechenden Antwortkästchens anzugeben. Danach werden Sie zum Fragebogen weitergeleitet. Das Ausfüllen des Screening-Fragebogens dauert in etwa 15 Minuten.

Zu den Ausschlusskriterien zählen beispielsweise:

- Das Vorliegen von Aspekten, welche gegen eine Untersuchung im fMRT sprechen würden:
  - elektrisch, magnetisch oder mechanisch gesteuerten Implantate (z.B. Herzschrittmacher),
  - intrakranielle Aneurysmaklammern,
  - eingesetzte metallische Implantate (insbes. Ferromagnetische Materialien), z.B. chirurgische Klammern, metallische Herzklappen, Knochenimplantate, Zahnimplantate (Amalgam- oder Goldfüllungen stellen kein Problem dar),
  - das Ausüben eines Berufs oder Tätigkeiten ausüben, bei denen Sie sich ferromagnetische Teile zugezogen haben könnten, oder wenn sich in Ihnen Metallsplitter befinden könnten,

- Permanent Make-up oder Gesichts-Tattoos,
- eine beeinträchtigte Thermoregulation,
- implantierte prothetische Herzklappen,
- klaustrophobische Veranlagung (d.h. wenn Sie starke Angstgefühle in engen und dunklen Räumen haben),

• Weitere Ausschlussgründe:

- aktuelle neurologische oder psychiatrische Krankheiten, oder schwere/chronische körperliche Erkrankungen,
- das Leiden an chronischen Schmerzen, oder an einer Erkrankung, welche die Schmerzverarbeitung beeinträchtigt,
- regelmäßige Medikamenteneinnahme (ausgenommen hormonelle Verhütungsmittel),
- eine Allergie gegen Rubriment Emulsion® oder einen der Inhaltsstoffe:

  Nikotinsäurebenzylester, Nonylsäurevanillylamid, Salicylsäure-monoglykolester, Salicylamid, Kampfer, Terpentinöl, Isobornylacetat, Emulg. Cetylstearylalkohol, Emulg. Cetylstearylalkohol mit Zusatz eines nichtionogenen Emulgators, Paraffinöl und Gereinigtes Wasser.
- das Leiden an einer Hauterkrankung (z.B. Neurodermitis, Schuppenflechte, …) oder wenn Sie eine überempfindliche Haut haben (z.B. sehr schnelle Sonnenbrandentwicklung),
- wenn Sie schwanger sind oder die Vermutung einer Schwangerschaft besteht.

Sofern Sie sich anhand Ihrer Angaben im Screening-Fragebogen für die Teilnahme an dieser Studie qualifizieren, werden Sie zum Testtermin eingeladen.

Testtermin:

Bitte sehen Sie einen Tag (24 Stunden) vor den Testungen davon ab Sport zu treiben, zu rauchen, Alkohol oder Drogen zu konsumieren oder Medikamente einzunehmen. Am Tag der Testungen bitten wir Sie, zwei Stunden vor Ihrem Termin ausschließlich Wasser zu trinken, und innerhalb dieser Zeit auf das Zähneputzen oder Kaugummikauen zu verzichten.

Zu Beginn des Testtermins wird ein weiteres Mal die Einverständniserklärung zur Studienteilnahme durchgegangen und unterzeichnet. Hierbei haben Sie nochmal die Möglichkeit weitere Fragen zum Inhalt der Teilnehmerinformationen und Einverständniserklärung zu stellen. Da der Untersuchungsgegenstand dieser Studie die Auswirkung anhaltender Schmerzen auf die Wahrnehmung der Schmerzen einer anderen Person ist, wird gemeinsam mit Ihnen noch eine weitere Person (ebenfalls StudienteilnehmerIn) an diesem Testtermin teilnehmen. Eine/r von Ihnen wird die Aufgaben dieser Testung im Magnetresonanztomographen und eine/r außerhalb an einem

Computer im Testraum nebenan zeitgleich durchführen. Die Person im Magnetresonanztomographen erhält eine Creme auf dem Unterarm aufgetragen. Diese Creme wird in 50% der Fälle eine durchblutungsfördernde Wärmesalbe sein (Rubriment Emulsion®), welche brennende Empfindungen leichter bis mittlerer Intensität erzeugt. In den anderen Fällen wird eine Placebo-Creme (hypoallergene Salbengrundlage, Ultrasicc®) aufgetragen. Diese enthält keine aktiven Wirkstoffe. Als TeilnehmerIn dieser Studie können Sie also einer von drei Gruppen zugeteilt werden:

- Studienteilnahme außerhalb des Scanners, keine Creme
- Studienteilnahme innerhalb des Scanners, Rubriment Emulsion®
- Studienteilnahme innerhalb des Scanners, Ultrasicc®

Die Zuteilung innerhalb oder außerhalb des Scanners, sowie der Cremes wurde mittels eines zufallsbasierten Computerskripts vorbestimmt und wird basierend auf der Reihenfolge Ihrer Studienanmeldung eingeteilt.

Nach dem Unterzeichnen der Teilnehmerinformationen erhalten Sie die Auskunft, ob Sie die Testung innerhalb des Scanners durchführen werden, oder außerhalb, im Testraum. Danach erhalten Sie die entsprechenden Instruktionen zu den Inhalten der Testung. Anschließend werden Sie gebeten, eine Urinprobe abzugeben. Dies dient der Überprüfung, dass Sie keine Drogen (z.B. Kokain, Opiate, Benzodiazepine, Amphetamine, Barbiturate, PCP) konsumiert haben und (falls Sie eine Frau sind) nicht schwanger sind. Diese Kontrolle ist eine Vorsichtsmaßnahme, da eine Untersuchung im MRT während des ersten Trimesters einer Schwangerschaft zu Forschungszwecken ein unnötiges Risiko darstellt und nicht gestattet ist. Der Drogentest dient dazu festzustellen, dass keine Substanzen konsumiert wurden, die einen Einfluss auf die Schmerzwahrnehmung nehmen könnten. Wenn Drogen- und Schwangerschaftstest negativ ausfallen, wird eine 10-minütige Entspannungsphase stattfinden.

Bitte beachten Sie, dass Rückstände von Cannabis bis zu drei Wochen nach Konsum noch im Urin messbar sind. Daher bitten wir Sie für diesen Zeitraum bis zum Testtermin vom Konsum abzusehen. Sollte der Drogentest positiv ausfallen, können wir Sie nicht als Versuchsperson inkludieren und müssen die Testung abbrechen.

Während der Testung werden die Gehirnaktivität im Magnetresonanztomographen (falls zugeteilt), Ihre Herzrate, die Hormonkonzentration Ihres Speichels und Ihre aktuelle Stimmung gemessen. Die Messung der Herzrate erfolgt ausschließlich während der Bearbeitung der Experimentalaufgaben. Im Magnetresonanztomographen wird hierzu eine MRT-kompatible Fingerclip-Elektrode angebracht, im Testraum werden Ihnen hingegen EKG-Elektroden angeklebt. Zur Ermittlung der Hormonkonzentration wird die Studienleitung Sie im Verlauf des Experimentes zweimal bitten, eine Speichelprobe abzugeben. Einmal zu Beginn des Experiments und einmal nach der Bearbeitung der Experimentalaufgaben. Die Speichelproben werden nach der Auswertung vernichtet. Die Messung Ihrer aktuellen Stimmung erfolgt über einen Fragebogen am Computer, welcher fünfmal im Verlauf des Testtermins vorgegeben wird.

Während der Messung im Magnetresonanztomographen oder am Computer im Testraum werden Sie zwei Aufgaben ausführen. Die Aufgaben umfassen eine Schmerzaufgabe (ca. 20 Minuten), während derer abwechselnd Ihnen oder der anderen Person schmerzhafte elektrische Reize über eine bipolare konzentrische Oberflächenelektrode auf Ihrem Handrücken verabreicht werden. Nach jeder Reizgabe werden Sie gebeten diese zu bewerten. Dabei bewerten Sie sowohl ihren eigenen Schmerz, als auch den der anderen Person anhand mehrerer Dimensionen (z.B. wie schmerzhaft, wie unangenehm). Die Schmerzreize werden mit einer Elektrode verabreicht und in einer Kalibrierungsprozedur individuell auf jede Versuchsperson und deren Schmerztoleranz angepasst. Die zweite Aufgabe ist eine Anstrengungsaufgabe (ca. 35 Minuten), bei der Sie entscheiden können, ob Sie mithilfe eines Handkraftmessers körperliche Anstrengung aufbringen möchten, um entweder für Sich selbst, oder die andere Person die Anzahl schmerzhafter Reize zu reduzieren. Nach jeder Entscheidung muss die gewählte Anstrengung sofort erbracht werden. Im Anschluss an die Anstrengungsaufgabe wird die erzielte Menge an Schmerzreizen aus drei zufälligen Runden verabreicht. Im Magnetresonanztomographen werden dabei die, bei diesen Aufgaben aktiven, Areale des Gehirns gemessen. Im Anschluss an die Experimentalaufgaben wird ein struktureller Scan des Gehirns angefertigt (7 Minuten). Die Dauer der fMRT-Messung beträgt maximal 90 Minuten (ca. 55 Minuten Experimentalaufgaben, 10 Minuten Stimmungsfragebögen, 7 Minuten struktureller Scan, 5 Minuten MRT-Einstellungen, inklusive Wartezeiten und Vorbereitungen).

Nach der Messung im Magnetresonanztomographen oder außerhalb am Computer werden Sie beide gebeten, Fragebögen auszufüllen. Diese beinhalten Fragen zu demographischen Daten, sowie einige Persönlichkeitsfragebögen. Zuletzt folgt eine vollständige Aufklärung über den Zweck der Studie und eine weitere Möglichkeit, Fragen zu stellen.

Ihre Teilnahme an dieser Studie wird einen Termin in Anspruch nehmen und insgesamt maximal 3 Std. dauern.

Die Einhaltung der Anweisungen des Studienleiters und seiner MitarbeiterInnen ist dabei von entscheidender Bedeutung für den Erfolg dieser Studie.

3. Worin liegt der Nutzen einer Teilnahme an der Studie?

Die Teilnahme an dieser Studie hat für Sie persönlich keinen unmittelbaren Nutzen. Die Ergebnisse dieser Studie sollen zeigen, wie sich anhaltende Schmerzen auf Ihr Verhalten bei den zu bearbeitenden Aufgaben auswirkt.

4. Gibt es Risiken, Beschwerden und Begleiterscheinungen?

Rubriment Emulsion®

Im Rahmen dieser Studie wird zur Auslösung anhaltender Schmerzen die Wärme-Creme Rubriment Emulsion® auf Ihrem Unterarm aufgetragen. Arzneimittel, wie Rubriment

Emulsion®, werden häufig gegen Durchblutungsstörungen, Muskelschmerzen oder Nervenschmerzen angewandt. Bei erstmaligem Auftragen hat diese Creme wärmende, juckreiz- und durchblutungsfördernde, gefäßerweiternde und reizende, brennende Eigenschaften. Die in dieser Studie verwendete einmalige Dosierung (3ml) überschreitet nicht die üblicherweise verabreichte Dosis bei PatientInnen, die diese Creme regelmäßig auftragen.

Aus diesem Grund ist das Risiko von unerwünschten Nebenwirkungen als gering einzuschätzen. Hinzu kommt, dass potentielle TeilnehmerInnen sehr genau auf mögliche Faktoren überprüft werden, die mit einem Risiko für unerwünschten Nebenwirkungen einhergehen, und gegebenenfalls von der Studie ausgeschlossen werden.

Falls Sie nach Verlassen des Labors Nebenwirkungen bemerken, können Sie uns jederzeit über die Studienmailadresse oder telefonisch kontaktieren .

Die Nebenwirkungen, die durch Rubriment Emulsion® verursacht werden können, sind hier angegeben:

Erkrankungen der Haut und des Unterhautzellgewebes.: Es sind verstärkte Hautreaktionen (Brennen, Quaddeln) möglich.

Elektrische Stimulation

Zur elektrischen Stimulation des Handrückens werden sehr kurze (500 ms) elektrische Schmerzreize verwendet, die über eine bipolare konzentrische Oberflächenelektrode verabreicht werden. Diese werden computergesteuert über ein Gerät gesteuert, bei dem es sich um ein CE-zertifiziertes Medizinprodukt handelt. Dieses Gerät ist für die Anwendung an Menschen zugelassen und wurde bereits in vielen Studien problemlos eingesetzt.

Die elektrische Stimulation des Handrückens kann eine leichte Rötung der Haut hervorrufen, die sich jedoch innerhalb kurzer Zeit zurückbildet. Die Methode wurde bereits vielfach angewandt und es sind keine Spätfolgen bekannt.

Magnetresonanztomographie

Die Magnetresonanztomographie (auch MRT, NMR oder Kernspintomographie genannt) erzeugt, ähnlich der Computertomographie, Schnittbilder des menschlichen Körpers. Sie benötigt im Gegensatz zu der Computertomographie keine Röntgenstrahlen, sondern lediglich ein starkes Magnetfeld und Radiowellen. Das physikalische Prinzip ist schon seit 1946 bekannt, seit Beginn der 80er Jahre wird es auch als diagnostisches Verfahren in der Medizin verwendet.

Die Untersuchung ist für ProbandInnen zwar völlig schmerzlos, jedoch laut. Aus diesem Grunde ist das Tragen eines Gehörschutzes (wird zur Verfügung gestellt) Bestandteil der Untersuchung. Gesundheitliche Risiken oder Nebenwirkungen sind bei den verwendeten Magnetfeldstärken bisher nicht beobachtet worden.

Wegen der extrem starken Magnetfelder (mehrere Tausendfache des Erdmagnetfeldes), die für dieses Verfahren benötigt werden, dürfen Personen mit Metallsplittern (z.B. Granatensplitter) nur eingeschränkt untersucht werden. Abhängig von den magnetischen Eigenschaften und ihrer Größe können Metalle im Körper ein Problem darstellen. Neben einer Bewegung der Metallobjekte durch das Magnetfeld kann es zu einer übermäßigen Erwärmung während der Untersuchung kommen. Feste Zahnimplantate können in der MRT in der Regel untersucht werden. Bei anderen metallischen Implantaten (künstliche Gelenke, Metallplatten nach Knochenbrüchen, etc.) muss im Einzelfall über die MRT-Tauglichkeit entschieden werden. Das Verrutschen eines Intrauterinpessars (Spirale) ist denkbar. Implantierte elektrische Aggregate wie etwa Herzschrittmacher, Insulinpumpen oder Nervenstimulatoren dürfen prinzipiell nicht in der MRT untersucht werden.

Sie befinden sich während der Untersuchung in einer relativ engen Röhre, dies kann bei Personen mit Platzangst eine Untersuchung erschweren. Während der Untersuchung können Sie sich jederzeit über eine Klingel bemerkbar machen, eine Gegensprechanlage erhält die Kommunikationsmöglichkeit mit den Studienleiter/innen aufrecht. Sie können die Untersuchung jederzeit abbrechen. Die eingestrahlten Radiowellen führen zu einer Erwärmung des Gewebes, dies ist zum Teil spürbar und kann entsprechend zum Schwitzen führen.

Das Wort „funktionell" bei der „funktionellen Magnetresonanztomographie" weist darauf hin, dass der „funktionelle" Zustand des Gehirns gemessen wird. Man misst hierbei den Sauerstoffverbrauch im Gehirn und zieht daraus Rückschlüsse, welche Gehirnareale gerade eine „Funktion" ausführen, also aktiv sind. Bei den im Rahmen dieser Studie durchgeführten Untersuchungen im Magnetresonanztomographen handelt es sich nicht um diagnostische Untersuchungen. Sollten sich dennoch Anhaltspunkte für ein krankhaftes Geschehen in Ihrem Gehirn ergeben, wird ein Radiologe konsultiert.

5. Zusätzliche Einnahme von Arzneimitteln?

Bitte teilen Sie jegliche Art von Medikamenten, welche Sie zurzeit einnehmen, der Studienleitung und/oder deren MitarbeiterInnen zur Abklärung mit. Sie sollten in den Tagen vor dieser Untersuchung keine anderen Medikamente, mit Ausnahme von Verhütungsmitteln oder Hormonpräparaten (diese bitte dennoch mitteilen) einnehmen. Wenn Sie dies doch getan haben, teilen Sie es bitte unbedingt dem Studienteam mit.

6. Hat die Teilnahme an der Studie sonstige Auswirkungen auf die Lebensführung und welche Verpflichtungen ergeben sich daraus?

Die Teilnahme hat keinerlei sonstige Auswirkungen auf die Lebensführung. Jedoch sollten Sie den folgenden Bitten unbedingt nachkommen:

2 Stunden vor dem Experiment
- nichts zu essen

- nur Wasser und keine koffeinhaltigen Getränke, z.B. Kaffee, Cola, Tee oder Säfte, zu trinken
- Ihre Zähne nicht zu putzen
- keinen Kaugummi zu kauen

24 Stunden vor dem Experiment
- keinen Sport mehr zu betreiben
- keinen Alkohol zu konsumieren
- keine Medikamente zu konsumieren

72 Stunden vor dem Experiment
- keine bewusstseinsverändernden Drogen zu konsumieren (Cannabis etwa 3 Wochen vor dem Experiment nicht mehr konsumieren)
- keine Schlafmittel (Benzodiazepine) einzunehmen

Da es sich bei dieser Studie um eine Untersuchung mittels Magnetresonanztomografie handelt, ist es zudem auch sehr wichtig, dass Sie währenddessen keine Metallteile am Körper tragen. Dazu zählen zum Beispiel:

- Metallschmuck (Uhren, Ketten, Armbänder, Ringe, Ohrringe, Piercings)
- Make-Up und Nagellacke (diese können Glitzerpartikel enthalten, es wird die Möglichkeit geben vor Ort beides zu entfernen)
- Gürtel
- BHs mit Metallbügel (Sport-BHs und Tops bieten sich als Alternativen an)

7. Was ist zu tun beim Auftreten von Symptomen, Begleiterscheinungen und/oder Verletzungen?

Sollten im Verlauf der Studie irgendwelche beschwerlichen Symptome, Begleiterscheinungen, Krankheiten oder Verletzungen auftreten, müssen Sie diese der Studienleitung und/oder deren MitarbeiterInnen mitteilen, bei schwerwiegenden Begleiterscheinungen umgehend.

Sie können uns per Mail über unsere Studienmailadresse (soc-pain23@univie.ac.at) kontaktieren, oder telefonisch unter: +43 (0)1 40070-2420 (Telefonnummer Fachbereich Radiologie).

Weitere Kontaktmöglichkeiten finden Sie unter Punkt 11.

8. Wann wird die Studie vorzeitig beendet?

Sie können jederzeit, auch ohne Angabe von Gründen, Ihre Teilnahmebereitschaft widerrufen und aus der Studie ausscheiden ohne dass Ihnen dadurch irgendwelche Nachteile entstehen.

Es ist aber auch möglich, dass Ihr Studienleiter entscheidet, Ihre Teilnahme an der Studie vorzeitig zu beenden, ohne vorher Ihr Einverständnis einzuholen. Die Gründe hierfür können sein:

a) Sie können den Erfordernissen der Studie nicht entsprechen;

b) Der Studienleiter hat den Eindruck, dass eine weitere Teilnahme an der Studie nicht in Ihrem Interesse ist;

9. Datenschutz

Im Rahmen dieser Studie werden Daten über Sie erhoben und verarbeitet. Es ist grundsätzlich zu unterscheiden zwischen

1) jenen personenbezogenen Daten, anhand derer eine Person direkt identifizierbar ist (z.B. Name, Geburtsdatum, Adresse, Sozialversicherungsnummer, Bildaufnahmen...),
2) pseudonymisierten personenbezogenen Daten, das sind Daten, bei denen alle Informationen, die direkte Rückschlüsse auf die konkrete Person zulassen, entweder entfernt, durch einen Code (z. B. eine Zahl) ersetzt oder (z.B. im Fall von Bildaufnahmen) unkenntlich gemacht werden. Es kann jedoch trotz Einhaltung dieser Maßnahmen nicht vollkommen ausgeschlossen werden, dass es unzulässigerweise zu einer Re-Identifizierung kommt.
3) anonymisierten Daten, bei denen eine Rückführung auf die konkrete Person ausgeschlossen werden kann.

Zugang zu den Daten, anhand derer Sie direkt identifizierbar sind (siehe Punkt 1), haben der Prüfarzt und andere Mitarbeiter des Studienzentrums, die an der klinischen Studie oder Ihrer medizinischen Versorgung mitwirken. Zusätzlich können autorisierte und zur Verschwiegenheit verpflichtete Beauftragte des Sponsors (Universität Wien)sowie Beauftragte von in- und/ oder ausländischen Gesundheitsbehörden und jeweils zuständige Ethikkommissionen in diese Daten Einsicht nehmen, soweit dies für die Überprüfung der ordnungsgemäßen Durchführung der klinischen Studie notwendig bzw. vorgeschrieben ist. Sämtliche Personen, die Zugang zu diesen Daten erhalten, unterliegen im Umgang mit den Daten den jeweils geltenden nationalen Datenschutzbestimmungen und/oder der EU-Datenschutz-Grundverordnung (DSGVO).

Der Code, der eine Zuordnung der pseudonymisierten Daten zu Ihrer Person ermöglicht, wird nur an Ihrem Studienzentrum aufbewahrt.

Eine Weitergabe der Daten, insbesondere an den Sponsor und seine Vertragspartner, erfolgt nur in pseudonymisierter oder anonymisierter Form.

Für etwaige Veröffentlichungen werden nur die pseudonymisierten oder anonymisierten Daten verwendet.

Im Rahmen dieser klinischen Studie ist auch eine Weitergabe von anonymisierten Daten weltweit und somit auch in Länder außerhalb der EU (Drittland) vorgesehen, diese Drittländer unterliegen nicht der DSGVO. Nicht für alle Drittländer liegt ein Angemessenheitsbeschluss vor, der ein gleichwertiges Datenschutzniveau gewährleistet, wie es in EU-Ländern aufgrund der DSGVO gegeben ist. Dadurch besteht das Risiko, dass Sie die Ihnen gemäß DSGVO zustehenden Rechte nicht durchsetzen können. Der Empfänger der Daten ist aber jedenfalls verpflichtet, Ihre Daten angemessen zu schützen. Wenn Sie an dieser klinischen Studie teilnehmen, stimmen Sie der Übermittlung Ihrer Daten in ein Drittland zu.

Ihre Einwilligung bildet die Rechtsgrundlage für die Verarbeitung Ihrer personenbezogenen Daten. Sie können die Einwilligung zur Erhebung und Verarbeitung Ihrer Daten jederzeit ohne Begründung widerrufen. Nach Ihrem Widerruf werden keine weiteren Daten mehr über Sie erhoben. Die bis zum Widerruf erhobenen Daten können allerdings weiter im Rahmen dieser klinischen Studie verarbeitet werden.

Nach der DSGVO stehen Ihnen grundsätzlich die Rechte auf Auskunft, Berichtigung, Löschung, Einschränkung der Verarbeitung, Datenübertragbarkeit und Widerspruch zu, soweit dies die Ziele der klinischen Studie nicht unmöglich macht oder ernsthaft beeinträchtigt und soweit dem nicht andere gesetzliche Vorschriften widersprechen.

Die voraussichtliche Dauer der klinischen Studie ist bis 01.09.2025. Die Dauer der Speicherung Ihrer Daten über das Ende oder den Abbruch der klinischen Studie hinaus ist durch Rechtsvorschriften geregelt.

Falls Sie Fragen zum Umgang mit Ihren Daten in dieser klinischen Studie haben, wenden Sie sich zunächst an Ihren Prüfarzt. Dieser kann Ihr Anliegen ggf. an die Personen, die für den Datenschutz verantwortlich sind, weiterleiten.

Kontaktdaten der Datenschutzbeauftragten der an dieser klinischen Studie beteiligten Institutionen:

Datenschutzbeauftragte/r der MedUni Wien: datenschutz@meduniwien.ac.at

Datenschutzverantwortliche/r des AKH: postdatenschutz@gesundheitsverbund.at

Datenschutzbeauftragte/r des Sponsors Universität Wien: dsba@univie.ac.at

Sie haben das Recht, bei der österreichischen Datenschutzbehörde eine Beschwerde über den Umgang mit Ihren Daten einzubringen (www.dsb.gv.at; E-Mail: dsb@dsb.gv.at).

Die Weitergabe der gesammelten, anonymisierten Daten weltweit erfolgt über das Open Science Framework (OSF https://osf.io/), dies ist eine Plattform, auf der Wissenschaftler/Innen anonymisierte Datensätze zur Verfügung stellen, um transparente Forschung zu fördern. Alle, im Rahmen dieser Studien gesammelten und anonymisierten Daten werden im OSF-Profil des Projekts gespeichert und öffentlich geteilt.

10. Entstehen für die Teilnehmer Kosten? Gibt es einen Kostenersatz oder eine Vergütung?

Durch Ihre Teilnahme an dieser Studie entstehen für Sie keine zusätzlichen Kosten. Als Vergütung für Ihren Zeitaufwand erhalten Sie nach erfolgter Teilnahme an der Untersuchung insgesamt **€ 50,-**.

11. Möglichkeit zur Diskussion weiterer Fragen

Für weitere Fragen im Zusammenhang mit dieser Studie stehen Ihnen Ihre Studienleitung und deren MitarbeiterInnen gern zur Verfügung. Auch Fragen, die Ihre Rechte als ProbandIn in dieser Studie betreffen, werden Ihnen gerne beantwortet.

Name	**Rolle**	**Telefon**	**Email**
Dr. André Gahleitner	Koordinierender Prüfarzt	+43(0)1 40070-2420	andre.gahleitner@meduniwien.ac.at
Univ.-Prof. Dr. Claus Lamm	Projektleiter	+431 4277 47130	Claus.lamm@univie.ac.at
Mag. Dr. Markus Rütgen	Verantwortlicher Datenaufnahme	+431 4277 9802006	Markus.ruetgen@univie.ac.at
Julia Braunstein, BSc. MSc	Verantwortliche Datenaufnahme	+431 4277 9802006	Julia.therese.braunstein@univie.ac.at

12. Sollten behandelnde Ärzte von der Teilnahme an der Studie informiert werden?

Bitte informieren Sie uns über alle aktuellen ärztlichen Behandlungen vor Studienbeginn bzw. sobald diese beginnen. Falls Sie unmittelbar nach der Testung von einem anderen Arzt behandelt werden, sollten Sie ihn darüber informieren, dass Sie unter Umständen eine geringe Dosis Rubriment® Emulsion aufgetragen erhalten haben.

13. Versicherung

Als Teilnehmer an dieser Studie besteht für Sie ein verschuldensunabhängiger Versicherungsschutz (Personenschadenversicherung), der alle Schäden abdeckt, die an Ihrem Leben oder Ihrer Gesundheit durch die an Ihnen durchgeführten Maßnahmen der Studie verursacht werden können; ausgenommen sind genetische Schäden. Die Versicherung wurde für Sie bei der Zürich Versicherungs-Aktiengesellschaft (Leopold-Ungar-Platz 2, 1190 Wien; Tel.: 01/501 25 1338) im Rahmen der AKH-Rahmenversicherung unter der Polizzennummer 07229622-2, abgeschlossen. Auf Wunsch können Sie in die Versicherungsunterlagen Einsicht nehmen.

Im Schadensfall können Sie sich direkt an den Versicherer wenden und Ihre Ansprüche selbstständig geltend machen. Für den Versicherungsvertrag ist österreichisches Recht anwendbar, die Versicherungsansprüche sind in Österreich einklagbar.

Um den Versicherungsschutz nicht zu gefährden müssen Sie dem Studienleiter - oder der oben genannten Versicherungsgesellschaft - eine Gesundheitsschädigung, die als Folge der Studie eingetreten sein könnte, unverzüglich mitteilen.

14. Einwilligungserklärung

Name der Versuchsperson:

Geb.Datum:

Ich erkläre mich bereit, an der Studie „Auswirkungen von Schmerzen auf Soziale Wahrnehmung" teilzunehmen. Ich bin darüber aufgeklärt worden, dass ich die Teilnahme ohne nachteilige Folgen, insbesondere für meine medizinische Betreuung, ablehnen kann.

Ich bin von Frau/Herrn..... ausführlich und verständlich über die klinische Studie, mögliche Belastungen und Risiken, sowie über Wesen, Bedeutung und Tragweite der klinischen Studie und die sich für mich daraus ergebenden Anforderungen aufgeklärt worden. Ich habe darüber hinaus den Text dieser Patientenaufklärung und Einwilligungserklärung, die insgesamt *13* Seiten umfasst, gelesen. Aufgetretene Fragen wurden mir von der Studienleitung verständlich und zufriedenstellend beantwortet. Ich hatte ausreichend Zeit, mich zu entscheiden. Ich habe zurzeit keine weiteren Fragen mehr.

Ich werde den ärztlichen Anordnungen, die für die Durchführung der klinischen Studie erforderlich sind, Folge leisten, behalte mir jedoch das Recht vor, meine freiwillige Mitwirkung jederzeit zu beenden, ohne dass mir daraus Nachteile, insbesondere für meine medizinische Betreuung, entstehen.

Ich stimme ausdrücklich zu, dass meine im Rahmen dieser klinischen Studie erhobenen Daten wie im Abschnitt „Datenschutz" dieses Dokuments beschrieben verarbeitet werden.

Eine Kopie dieser Patienteninformation und Einwilligungserklärung habe ich erhalten. Das Original verbleibt beim Prüfarzt/der Studienleitung.

.....
(Datum und Unterschrift der Versuchsperson)

.....
(Datum, Name und Unterschrift der Studienleitung)

(Die Versuchsperson erhält eine unterschriebene Kopie der Patienteninformation und Einwilligungserklärung, das Original verbleibt im Studienordner des Prüfarztes/der Studienleitung.)

Appendix C

Post-experimental questions:

"Did you have any doubts about the experiment as a whole? If yes, which?"

"How did you experience the behaviour of the experimenters?"

Confederate

"How did you perceive the other person? "

"5-point Likert ratings on: similarity, strength, closeness, sympathy, pleasantness, neediness"

"Did you have any doubts about the other person? If yes, which?"

Empathy for pain paradigm

"What do you think was the goal of the pain task?"

"Did you use any specific strategies during this task? If yes, which?"

Prosocial Effort Task

"What do you think was the goal of the effort task?"

"Did you use any specific strategies during this task? If yes, which?"

"What was your main motivator for your decisions in this task?"

Appendix D

Pre-& Post-Study Questionnaires

Before admission to the study, participants were asked to fill out a number of questionnaires. Table 1 lists the different questionnaires and gives a quick overview of the factors assessed. Table 2 list the questionnaires filled out after the experiment's completion

Table D1

Pre-Study Questionnaires

Psychometric Tool	***Description***
The Autism-Spectrum Quotient **(AQ; Baron-Cohen, 2001)**	Used as assessment tool for autism symptoms. ASD (Autism Spectrum Disorder) has been shown to affect empathy (Hamsen, 2018) and prosocial behaviour (Zhang et al., 2024) as well as pain perception (Bogdanova et al., 2022) in a complex manner, which is not yet well understood.
Fear of Pain Questionnaire III **(FPQ-III, McNeil & Rainwater, 1998)**	Used to assess fear of pain. Fear of pain has been indicated in prior research to influence pain perception and top-down analgesic effects (Aristi et al., 2022; Lyby, Aslaksen, & Flaten, 2010; Lyby, Aslaksen, & Flaten, 2011; Romualdo et al., 2024).
Toronto Alexithymia Scale **(TAS-26, Kupfer, Brosig &, Brähler, 2000)**	The German version of the Toronto Alexithymia Scale (Kupfer, Brosig &, Brähler, 2001) was used to evaluate symptoms of alexithymia. Alexithymia generally describes the difficulty identifying or describing one's own emotions.

Table D2

Post Study Questionnaires

Psychometric Tool	***Description***
***Beck-Depression-Inventory II* (BDI–II, dt. Version: Hautzinger, Keller & Kühner, 2. Aufl.)**	Used to assess depression symptoms**.** Depression has been shown to influence empathic reactions (Guhn et al., 2020) as well as effort-based decision-making (Vinckier et al., 2022).
***Questionnaire of Cognitive and Affective Empathy* (QCAE, Reniers et al., 2011)**	Used as an assessment tool for trait cognitive and affective empathy

Appendix E

Behavioural Model Assumptions

Model fit and assumptions were checked utilising DHARMa package (Hartig, 2022). Scaled residuals were additionally visually inspected for systematic deviation from uniformity, homoscedasticity, and normality.

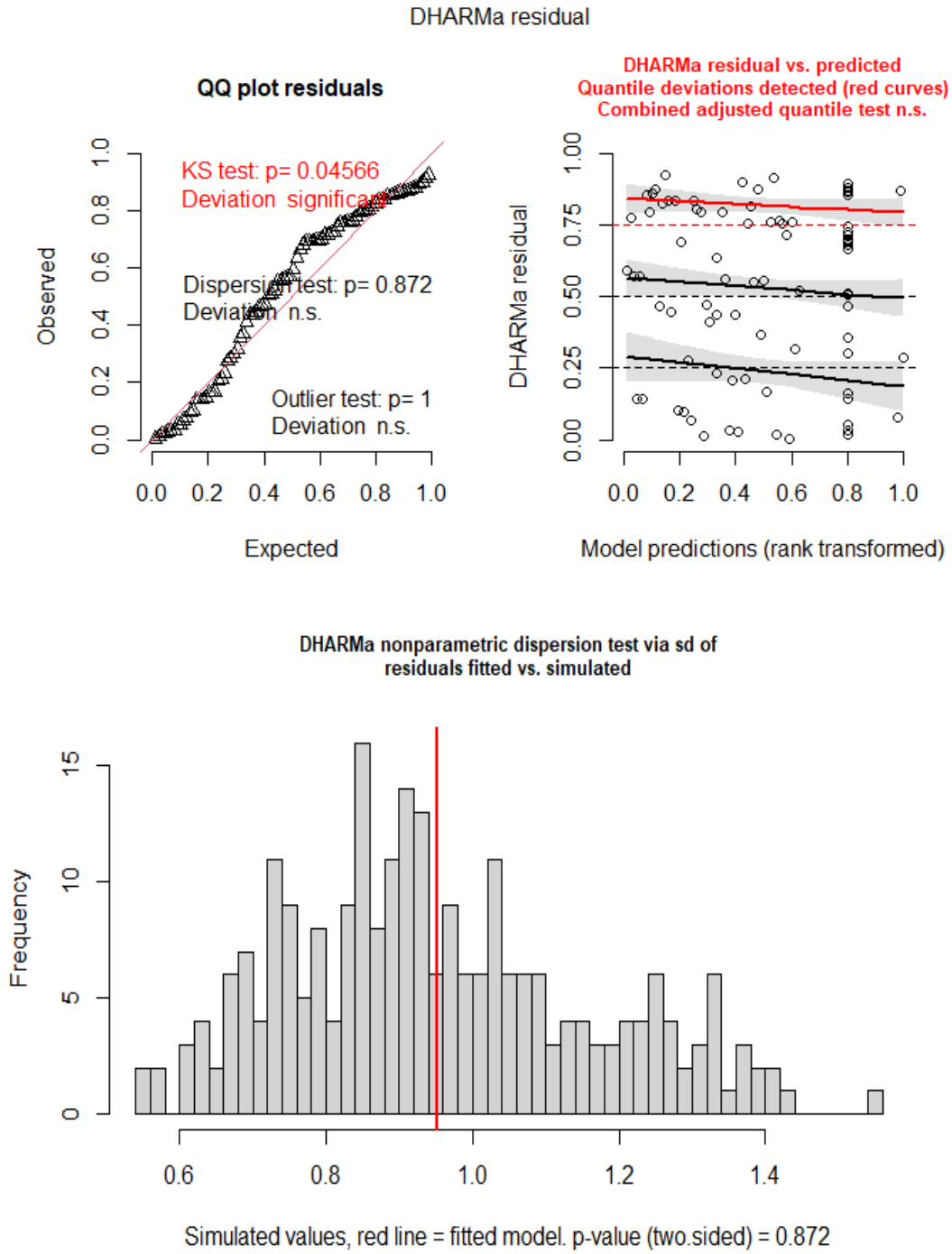
A slight but significant deviation from uniformity was detected using the Kolmogorov-Smirnov test for uniformity. However, upon visual inspection, no systematic skew or pattern was detected, indicating no substantial deviation.

Dispersion ($p = 0.87$) and homoscedasticity tests ($p = 0.87$) indicate an acceptable variance structure. No outliers were detected by the DHARMa outlier test. A few data points were flagged as potentially influential (Cook's distance > 0.05; IDs 16, 18, 19, 21, 36, and 62). While the striped model had a slightly better fit, the changes in estimates were not meaningful enough to accept the loss in power given the already small data set. (Full model: AIC (weights): 364.7 (<.001), AICc (weights): 366.0 (<.001), BIC (weights): 382.6 (<.001), R^2 (cond.): 0.638, R^2 (marg.): 0.031, ICC: 0.626, RMSE: 0.969, Sigma: 1.172 | stripped model: AIC (weights): 336.3 (>.999), AICc (weights): 337.7 (>.999), BIC (weights): 353.7 (>.999), R^2 (cond.): 0.688, R^2 (marg.): 0.038, ICC: 0.675, RMSE: 0.902, Sigma: 1.100). The *compare_performance* function from the *performance* R-package (Lüdecke et al., 2021) was used for model comparison.

The Variance Inflation Factor Test (VIF) indicates moderate multicollinearity between the PE (VIF = 9.439816) and PR (VIF = 9.426638). This is expected to a certain extent since participants are more likely to choose a higher effort option if the reward is also higher; additionally, both indices are averaged over the trial level, amplifying correlations.

Figure E1a-c

Behavioural Model Assumption Checks

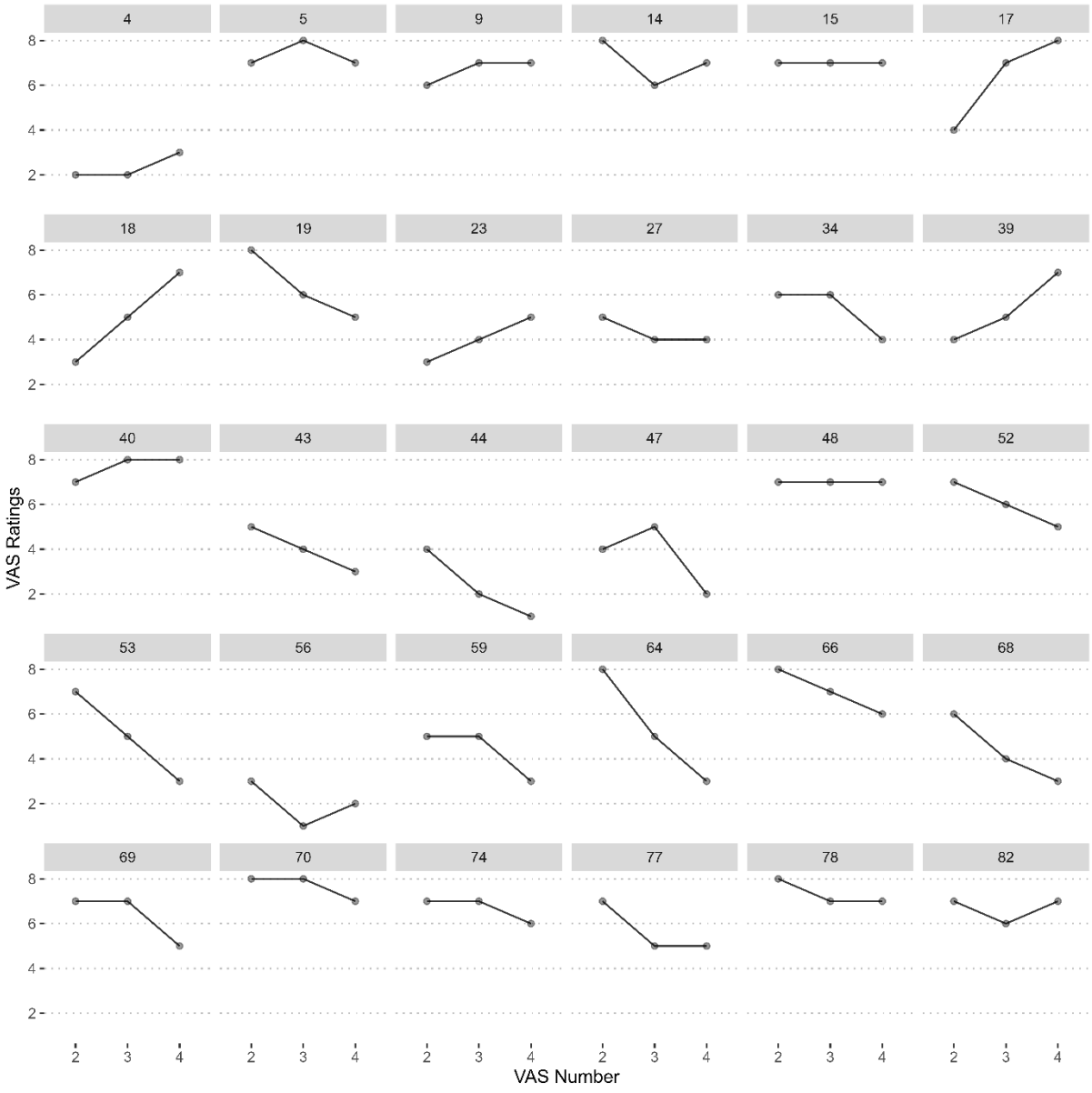


Appendix F

Descriptive Analysis

Figure F1

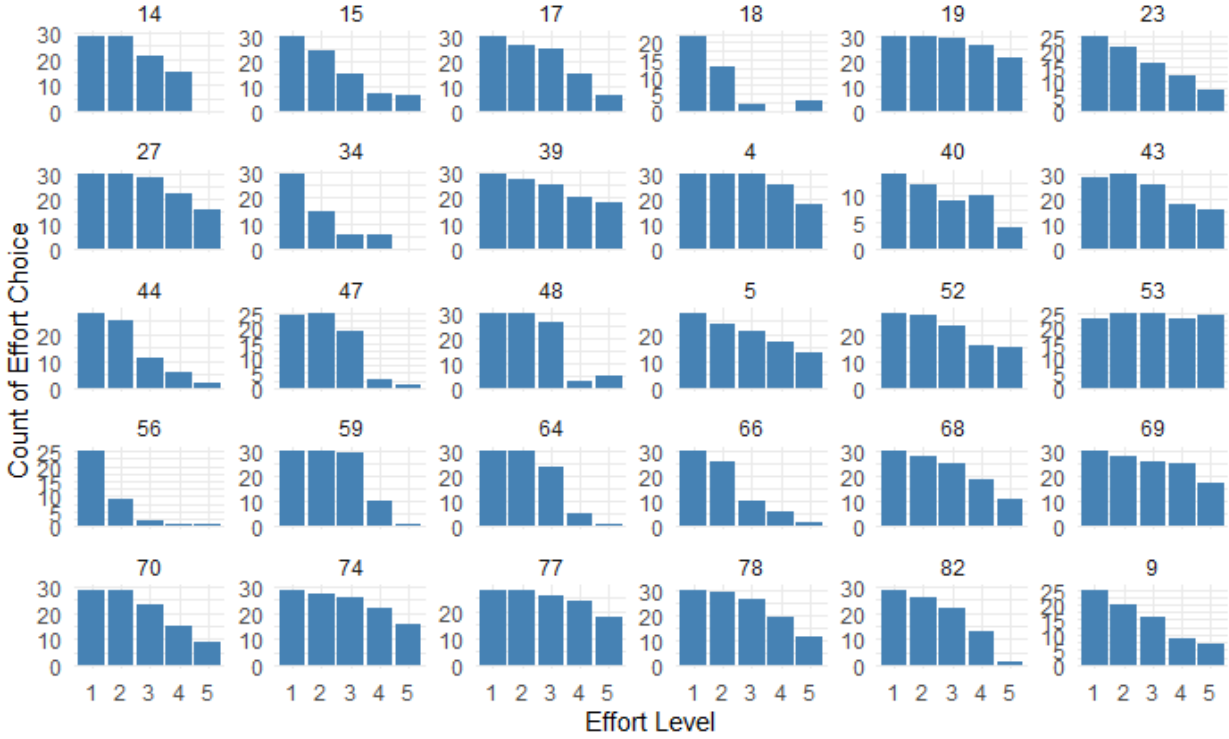
Pain Ratings Over Time per ID



Note: VAS pain ratings per participants across the analysed timepoints

Figure F2a

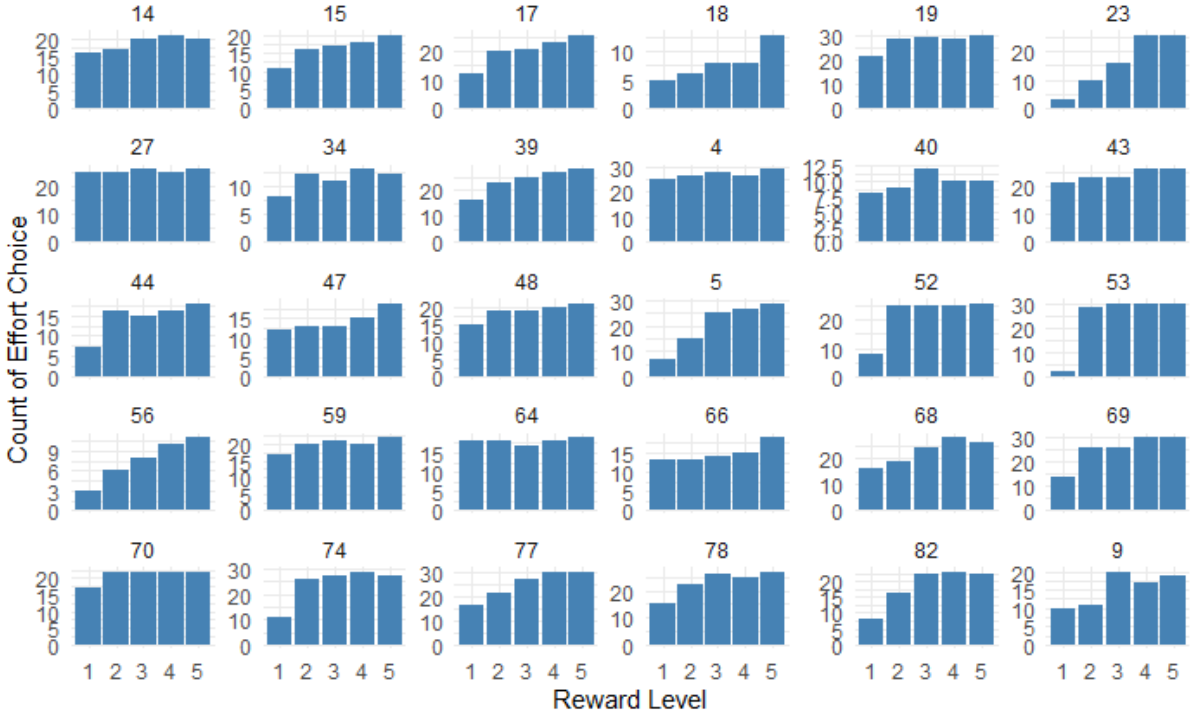
Distribution of Effort Choices per Effort Level per ID



Note: Bar-plots showing every participants' distribution of effort choices per effort level. The number displayed above each plot is the participants` anonymized ID.

Figure F2b

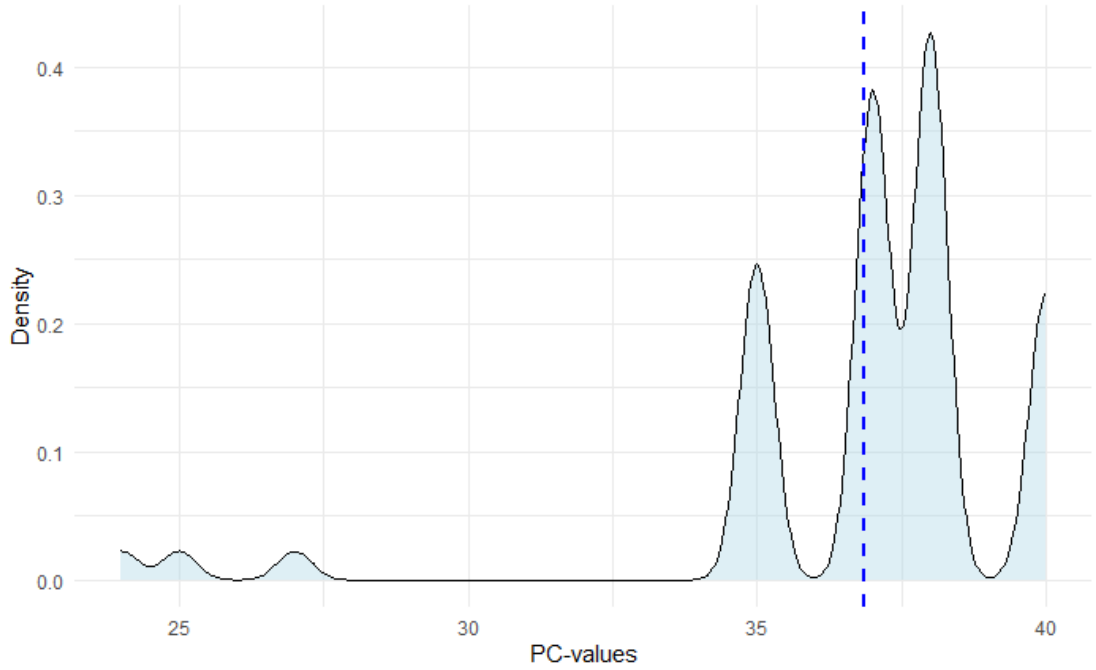
Distribution of Effort Choices per Effort Level per ID



Note: Bar-plots showing every participants' distribution of effort choices per reward level. The number displayed above each plot is the participants` anonymized ID.

Figure F3a

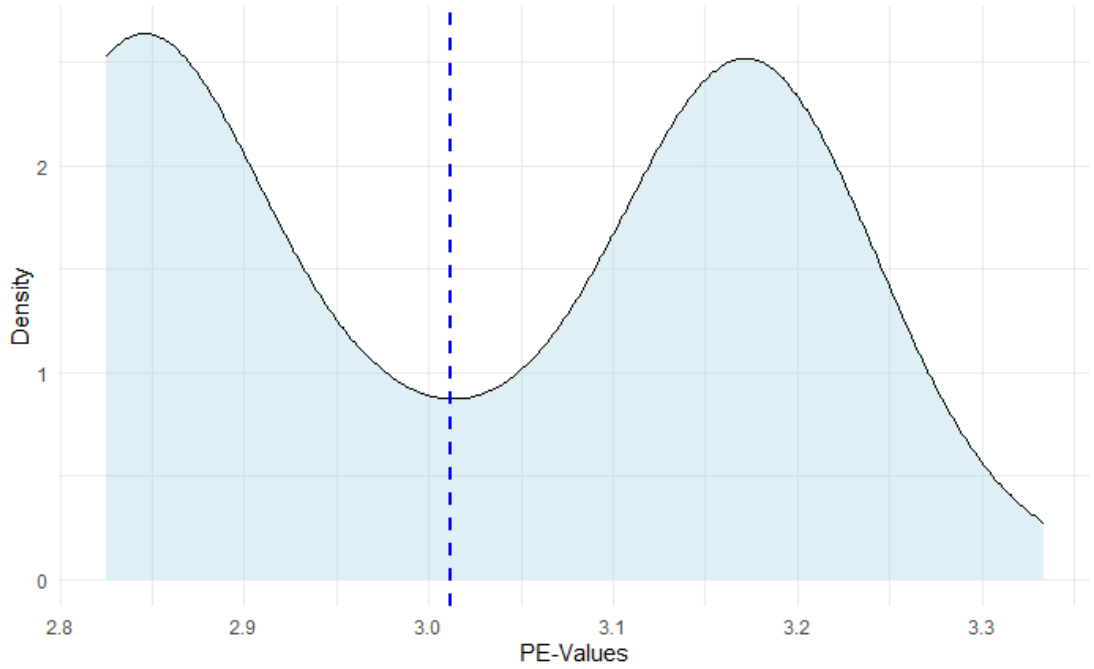
Density Distribution of PC



Note: The dashed line represents the mean of the distribution

Figure F3b

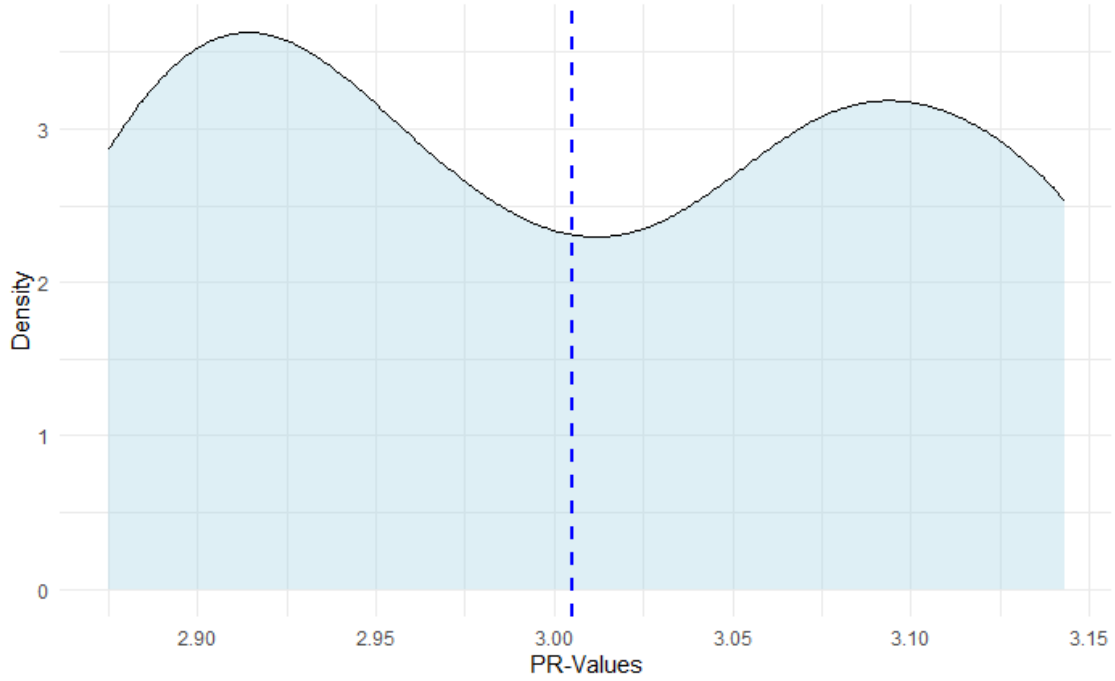
Density Distribution of PE



Note: The dashed line represents the mean of the distribution

Figure F3c

Density Distribution of PR



Note: The dashed line represents the mean of the distribution